
Supplementary information

**Photocatalytic oxygen-atom transmutation
of oxetanes**

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Supplementary Information

Photocatalytic oxygen-atom transmutation of oxetanes

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Table of contents

1. General.....	3
Solvents.....	4
Substrates	4
2. Supplementary Tables.....	29
Supplementary Table 1. Evaluation of reaction conditions.	29
Supplementary Table 2. Evaluation of reaction parameters.	30
Supplementary Table 3. Unsuccessful studies using Vilsmeier-Haack reagents and Appel reaction conditions.	31
3. Photocatalytic Oxygen-Atom Transmutation	32
Experimental procedures	32
4. Late-Stage Editing and Applications	80
Late-stage editing with densely functionalized bioactive amines.....	80
Late-stage editing of complex bioactive oxetanes	85
O-to-C transmutation to afford 1,1-difluorocyclobutane isostere.....	88
Synthesis of the key precursor of respiratory syncytial virus inhibitor	90
Synthesis of the key precursor of cyclin-dependent kinase 2 inhibitor	93
5. Mechanistic Investigations.....	96
Control experiments to probe dibromide intermediate	96
Control experiments to probe alkyl formate intermediate	97
6. Density Functional Theory (DFT) Calculations	98
Computational methods	98
Model reaction	99
Conformational Considerations	99

Most favourable pathway.....	100
Oxetane reactivity with complex I	101
Chemoselectivity between cyclic and acyclic ethers	102
DFT-optimised structures	104
Molecular origins of chemoselectivity.....	107
Simple transition state theory (TST) for rate estimation	112
Fukui reactivity index calculation.....	113
Optimised structures and absolute energies	113
7. NMR Spectra	116
8. X-ray Crystallographic Data	234
9. References.....	240

1. General

All commercial reagents were used without additional purification, unless otherwise stated. Anhydrous solvents were purchased from commercial sources and transferred under an argon atmosphere. ^1H NMR spectra were recorded on Bruker 300 MHz, Bruker 400 MHz and Bruker DPX 500 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance resulting from incomplete deuterium incorporation as the internal standard (CDCl_3 : δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, qd = quartet of doublets, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on Bruker 300 MHz, Bruker 400 MHz and Bruker DPX 500 MHz spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl_3 : δ 77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker 400 MHz and Bruker DPX 500 MHz spectrometer. High-resolution mass spectrometric data were obtained using Agilent 7200 Q-TOF, Bruker MicroTOF-QII and Waters Xevo G2-XS QToF. GC-MS analysis was performed on Shimadzu GCMS-QP2020 gas chromatography coupled to a Shimadzu QP2010 mass selective detector. Column chromatography purification conditions are reported in the experimental section below.

Photocatalytic reactions were performed with 2×456 nm Kessil lamps (PR160L-456 nm, 40 W, 25% intensity), equipped with a fan cooling system (the thermostat was set at 20-25 °C) and a magnetic stirrer (~ 600 rpm).



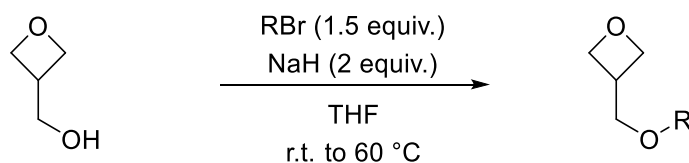
Solvents

Solvents (dichloromethane, tetrahydrofuran, acetonitrile and toluene) were purified under a positive pressure of dry nitrogen gas by a modified Innovative Technologies purification system. DMF (Sigma-Aldrich), DMSO (Sigma-Aldrich), cyclohexane (Sigma-Aldrich) methanol (Fisher), hexanes (Fisher) and ethyl acetate (Fisher) were used as received. All purification procedures of products were carried out with reagent grade solvents.

Substrates

General procedures for the preparation of oxetane substrates

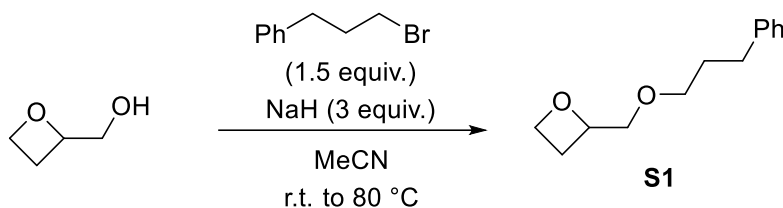
Method A:



To a solution of the oxetan-3-ylmethanol (1 mmol, 1 equiv.) in dried THF under N₂ atmosphere at room temperature, NaH (60 % dispersion in mineral oil, 2 mmol, 2 equiv.) was added dropwise. The mixture was allowed to stir for 30 min at room temperature. Then, the bromoalkane (1.5 mmol, 1.5 equiv.) was added in one portion and the mixture was allowed to stir overnight at 60 °C. After completion of the reaction, the reaction

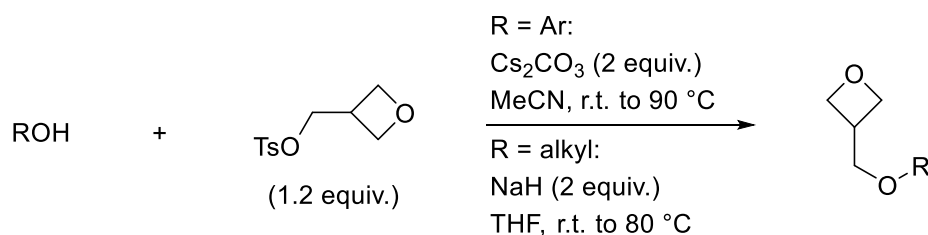
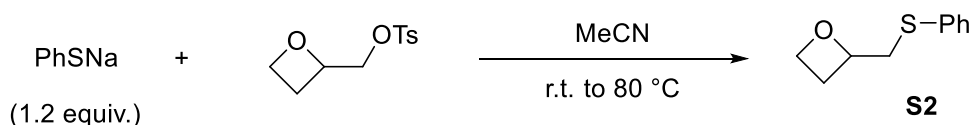
was quenched with saturated solution of NH_4Cl . The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford the oxetane.

Method B:



To a solution of the oxetan-2-ylmethanol (1 mmol, 1 equiv.) in dried MeCN under N_2 atmosphere at room temperature, NaH (60 % dispersion in mineral oil, 3 mmol, 3 equiv.) was added dropwise. The mixture was allowed to stir for 30 min at room temperature. Then, (3-bromopropyl)benzene (1.5 mmol, 1.5 equiv.) was added in one portion and the mixture was allowed to stir overnight at 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH_4Cl . The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 5:1) to afford the oxetane.

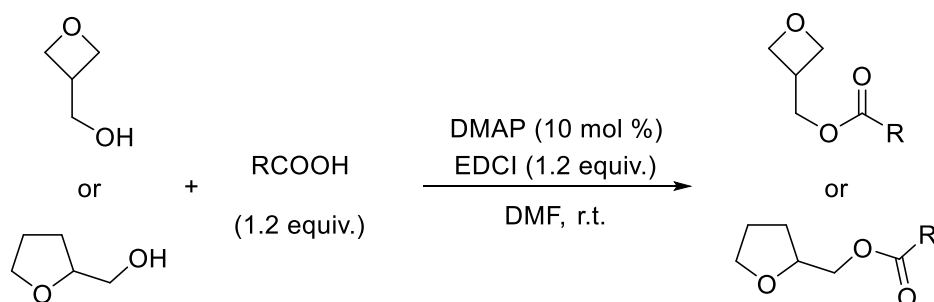
Method C:



For sulfur nucleophile: A solution of nucleophile sodium thiophenolate (1.2 mmol, 1.2 equiv.) and the corresponding TsO-substituted oxetane (1 mmol, 1 equiv.) in dried MeCN was prepared at room temperature. The mixture was allowed to stir overnight under 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 5:1) to afford the desired oxetane **S2**.

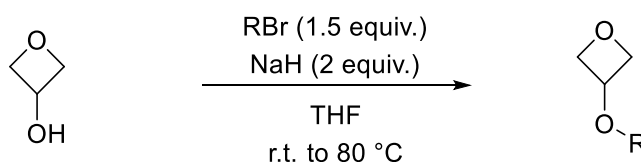
For oxygen pronucleophiles: To a solution of the pronucleophile ArOH (1 mmol, 1 equiv.) and TsO-substituted oxetane (1.2 mmol, 1.2 equiv.) in dried MeCN, Cs₂CO₃ (2 mmol, 2 equiv.) was added in one portion at room temperature. The mixture was allowed to stir overnight under 90 °C. For aliphatic alcohol pronucleophile, to a solution of the alcohol (1 mmol, 1 equiv.) in dried THF, NaH (60 % dispersion in mineral oil, 2 mmol, 2 equiv.) was added dropwise at room temperature. The mixture was allowed to stir for 30 min at room temperature. Then, the TsO-substituted oxetane (1.2 mmol, 1.2 equiv.) was added in one portion and the mixture was allowed to stir overnight at 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired oxetane.

Method D:



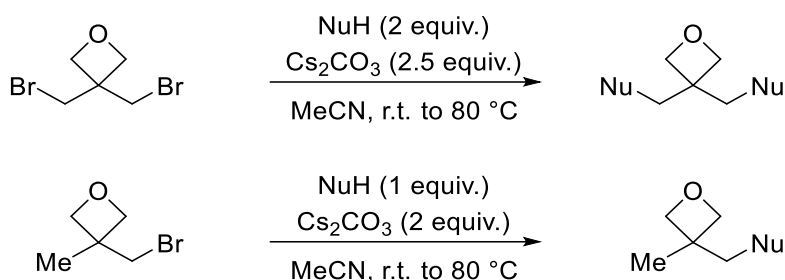
To a solution of oxetan-3-ylmethanol or (tetrahydrofuran-2-yl)methanol (1 mmol, 1 equiv.), DMAP (0.1 mmol, 0.1 equiv.) and EDCI (1.2 mmol, 1.2 equiv.) in DMF (1 mL) was added the corresponding carboxylic acid (1.2 mmol, 1.2 equiv.). The mixture was allowed to stirred for 3 h. After completion of the reaction, the solution was quenched with aqueous 1M HCl solution. The residue was extracted with EtOAc and the organic layer was then washed with NaHCO₃ followed by brine and dried over anhydrous Na₂SO₄. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired product.

Method E:



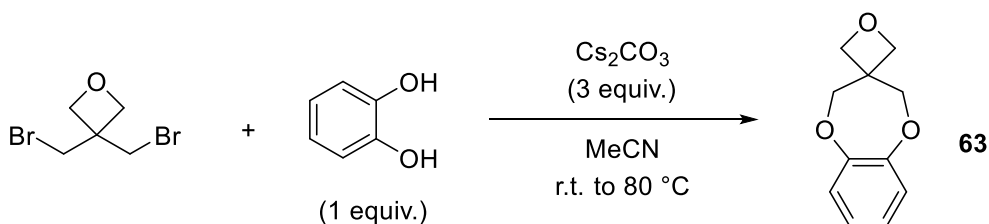
To a solution of oxetan-3-ol (1 mmol, 1 equiv.) in dried THF (1 mL), NaH (60 % dispersion in mineral oil, 2 mmol, 2 equiv.) was added dropwise at room temperature. Then, the mixture was allowed to stir for 30 min at room temperature. The bromoalkane (1.5 mmol, 1.5 equiv.) was added in one portion and the mixture was allowed to stir overnight at 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired product.

Method F:



To a solution of 3,3-bis(bromomethyl)oxetane (1 mmol, 1 equiv.) and corresponding nucleophile (2 mmol, 2 equiv.) in dried MeCN, Cs₂CO₃ (2.5 mmol, 2.5 equiv.) was added in one portion at room temperature. The mixture was allowed to stir overnight under 80 °C. The reaction of 3-(bromomethyl)-3-methyloxetane follows the above procedure with less nucleophile (1 mmol, 1 equiv.) and Cs₂CO₃ (2 mmol, 2 equiv.). After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired oxetane.

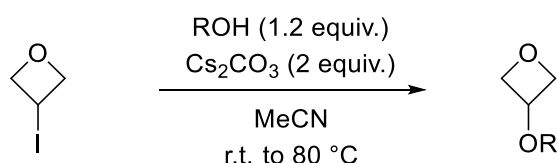
Method G:



To a solution of 3,3-bis(bromomethyl)oxetane (1 mmol, 1 equiv.) and pyrocatechol (1 mmol, 1 equiv.) in dried MeCN, Cs₂CO₃ (3 mmol, 3 equiv.) was added in one portion at room temperature. The mixture was allowed to stir for 3 h under 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified

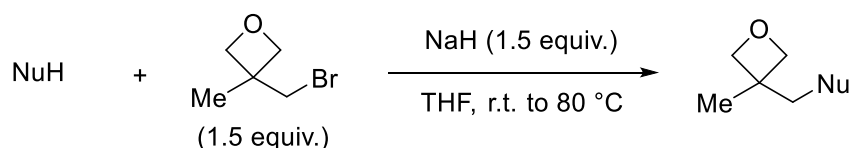
by column chromatography (silica gel, hexanes:EtOAc = 5:1) to afford the desired oxetane.

Method H:



To a solution of 3-iodooxetane (1 mmol, 1 equiv.) and the corresponding nucleophile ROH (1.2 mmol, 1.2 equiv.) in dried MeCN, Cs₂CO₃ (2 mmol, 2 equiv.) was added in one portion at room temperature. The mixture was allowed to stir overnight under 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired oxetane.

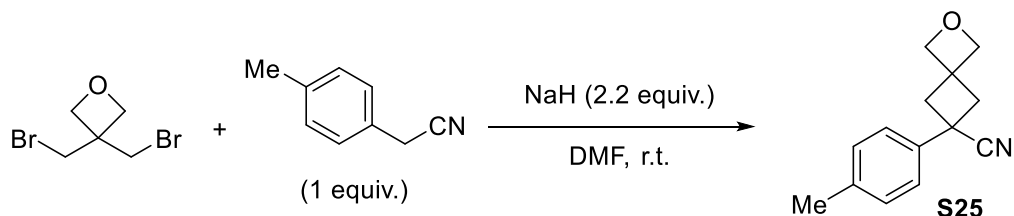
Method I:



To a solution of the nucleophile (1 mmol, 1 equiv.) in dried THF (1 mL), NaH (60 % dispersion in mineral oil, 1.5 mmol, 1.5 equiv.) was added dropwise at room temperature. Then, the mixture was allowed to stir for 30 min at room temperature. The 3-(bromomethyl)-3-methyloxetane (1.5 mmol, 1.5 equiv.) was added in one portion and the mixture was allowed to stir overnight at 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and

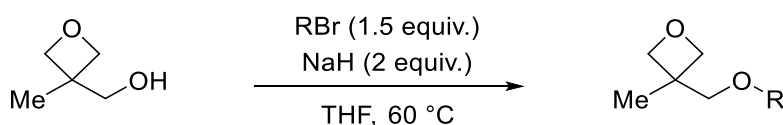
concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1 – 2:1) to afford the desired product.

Method J:



To a solution of NaH (60 % dispersion in mineral oil, 2.2 mmol, 2.2 equiv.) in dry THF (1 mL), 2-(*p*-tolyl)acetonitrile (1 mmol, 1 equiv.) was added dropwise at room temperature. Then, 3,3-bis(bromomethyl)oxetane (1 mmol, 1 equiv.) was added in one portion and the mixture was allowed to stir overnight at room temperature. After completion of the reaction, the reaction was quenched with saturated solution of NH_4Cl . The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 5:1) to afford the desired product.

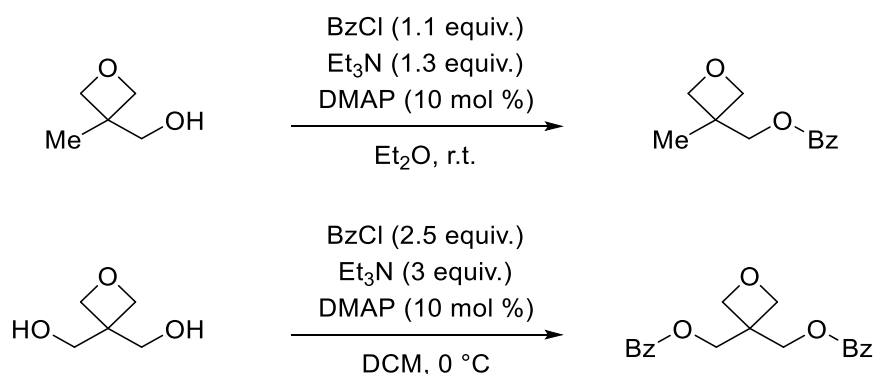
Method K:



To a solution of (3-methyloxetan-3-yl)methanol (1 mmol, 1 equiv.) in dry THF (1 mL), NaH (60 % dispersion in mineral oil, 2 mmol, 2 equiv.) was added dropwise at room temperature. The mixture was allowed to stir for 40 min at room temperature. Then, bromoalkane (1.5 mmol, 1.5 equiv.) was added in one portion and the mixture was allowed to stir overnight at 60 °C. After completion of the reaction, the reaction was

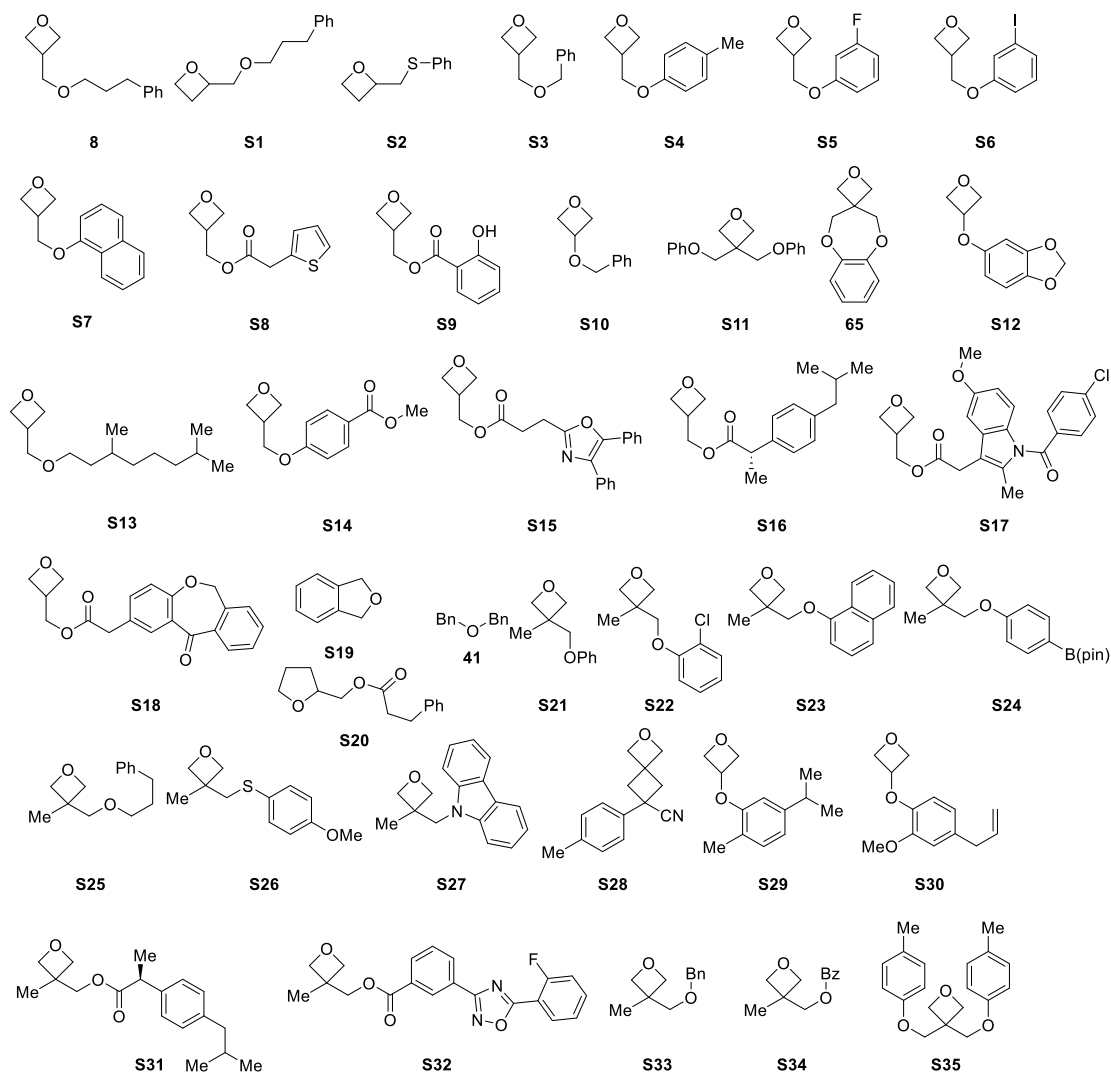
quenched with saturated solution of NH_4Cl . The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford the desired product.

Method L:



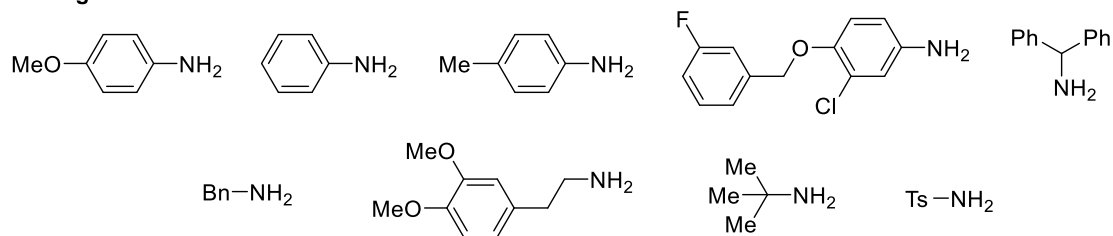
To a solution of (3-methyloxetan-3-yl)methanol (1 mmol, 1 equiv.), Et_3N (1.3 mmol, 1.3 equiv.) and DMAP (0.1 mmol, 10 mol %) in dry Et_2O (1 mL), BzCl (1.1 mmol, 1.1 equiv.) were added in one portion at room temperature. The mixture was allowed to stir at room temperature overnight. The analogous reaction of oxetane-3,3-diyl dimethanol follows the above procedure with more BzCl (2.5 mmol, 2.5 equiv.) and Et_3N (3 mmol, 3 equiv.) in DCM at $0\text{ }^\circ\text{C}$. After completion of the reaction, the reaction was quenched with saturated solution of NH_4Cl . The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford the desired product.

Scope 1 of ether substrates:



Scope 2 of commercially available nitrogen/sulfur/carbon/dual-atom reagents:

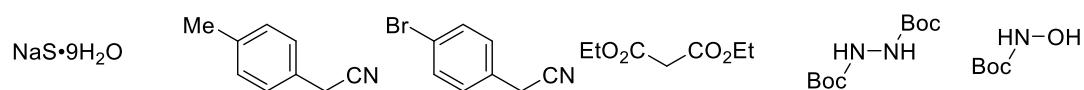
N reagents:



S reagents:

C reagents:

dual-atom reagents:

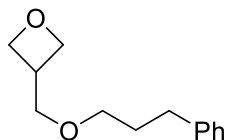


1,3-Dihydroisobenzofuran (**S19**, BLD pharm), (oxybis(methylene))dibenzene (**41**, BLD pharm), 4-methoxyaniline (Alfa Chemistry), aniline (Sigma-Aldrich), *p*-toluidine (Sigma-Aldrich), 3-chloro-4-((3-fluorobenzyl)oxy)aniline (BLD pharm), diphenylmethanamine (BLD pharm), phenylmethanamine (Apollo), 2-(3,4-dimethoxyphenyl)ethan-1-amine (TCI), 2-methylpropan-2-amine (Sigma-Aldrich), 4-methylbenzenesulfonamide (Sigma-Aldrich), sodium sulfide nonahydrate (Sigma-Aldrich), 2-(*p*-tolyl)acetonitrile (BLD pharm), 2-(4-bromophenyl)acetonitrile (BLD pharm), diethyl malonate (Sigma-Aldrich), di-*tert*-butyl hydrazine-1,2-dicarboxylate (BLD pharm), *tert*-butyl hydroxycarbamate (BLD pharm), CBr₄ (Sigma-Aldrich) and Ru(bpy₃)Cl₂·6H₂O (BLD pharm) are commercially available.

(**S8**)¹, (**S24**)² are known compounds with available analytical data.

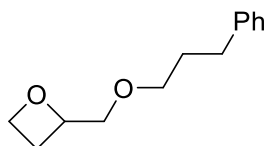
Analytical data of oxetane substrates

3-((3-phenylpropoxy)methyl)oxetane (**8**)



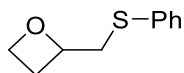
This compound was prepared according to **Method A** in 76% yield (156.6 mg) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.17 (m, 2H), 7.11 (td, *J* = 5.6, 3.1 Hz, 3H), 4.73 (dd, *J* = 7.8, 6.1 Hz, 2H), 4.38 (t, *J* = 6.0 Hz, 2H), 3.58 (d, *J* = 6.9 Hz, 2H), 3.38 (t, *J* = 6.4 Hz, 2H), 3.21 – 3.08 (m, 1H), 2.67 – 2.55 (m, 2H), 1.88 – 1.75 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 141.8, 128.4, 128.3, 125.8, 74.7, 72.5, 70.3, 35.0, 32.2, 31.1; HRMS (ESI) *calcd.* for (C₁₃H₁₉O₂) [M+H]⁺ : 207.1380, *found* 207.1381.

2-((3-phenylpropoxy)methyl)oxetane (**S1**):



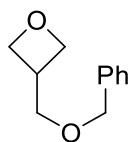
This compound was prepared according to **Method B** in 84% yield (173.5 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.35 – 7.29 (m, 2H), 7.22 (d, J = 7.7 Hz, 3H), 5.03 – 4.94 (m, 1H), 4.74 – 4.66 (m, 1H), 4.59 (dt, J = 9.0, 6.0 Hz, 1H), 3.67 – 3.51 (m, 4H), 2.77 – 2.53 (m, 4H), 2.01 – 1.92 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 142.0, 128.5, 128.3, 125.7, 81.2, 74.2, 70.8, 68.9, 32.3, 31.3, 23.8; **HRMS (ESI)** *calcd.* for (C₁₃H₁₈NaO₂) [M+Na]⁺ : 229.1199, *found*: 229.1203.

2-((phenylthio)methyl)oxetane (S2):



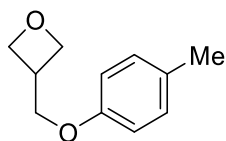
This compound was prepared according to **Method C** in 66% yield (118.8 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.44 – 7.38 (m, 2H), 7.34 – 7.26 (m, 2H), 7.25 – 7.19 (m, 1H), 4.98 – 4.87 (m, 1H), 4.72 – 4.62 (m, 1H), 4.62 – 4.53 (m, 1H), 3.31 (dd, J = 13.5, 5.5 Hz, 1H), 3.21 (dd, J = 13.5, 7.3 Hz, 1H), 2.74 (dtd, J = 11.3, 7.9, 6.0 Hz, 1H), 2.45 (ddt, J = 11.3, 9.1, 7.2 Hz, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 135.5, 129.9, 128.9, 126.4, 80.1, 68.2, 40.5, 27.1; **HRMS (ESI)** *calcd.* for (C₁₀H₁₃OS) [M+H]⁺ : 181.0682, *found*: 181.0685.

3-((benzyloxy)methyl)oxetane (S3):



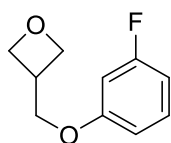
This compound was prepared according to **Method A** in 92% yield (163.8 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.50 – 7.26 (m, 5H), 4.80 (dd, J = 7.8, 6.1 Hz, 2H), 4.55 (s, 2H), 4.46 (t, J = 6.0 Hz, 2H), 3.71 (d, J = 6.9 Hz, 2H), 3.35 – 3.17 (m, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 138.0, 128.4, 127.7(0), 127.6(5), 74.6, 73.2, 71.7, 34.9; **HRMS (ESI)** *calcd.* for (C₁₁H₁₅O₂) [M+H]⁺ : 179.1067, *found* 179.1067.

3-((*p*-tolyl)oxy)methyl)oxetane (S4):



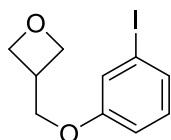
This compound was prepared according to **Method C** in 88% yield (156.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.13 – 7.06 (m, 2H), 6.86 – 6.78 (m, 2H), 4.88 (dd, *J* = 7.8, 6.2 Hz, 2H), 4.57 (t, *J* = 6.0 Hz, 2H), 4.17 (d, *J* = 6.7 Hz, 2H), 3.56 – 3.27 (m, 1H), 2.30 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 156.6, 130.3, 129.9, 114.3, 74.3, 69.3, 34.6, 20.4; **HRMS (ESI)** *calcd.* for (C₁₁H₁₅O₂) [M+H]⁺ : 179.1067, *found* 179.1068.

3-((3-fluorophenoxy)methyl)oxetane (S5):



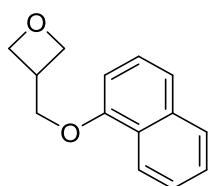
This compound was prepared according to **Method C** in 80% yield (145.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.23 (td, *J* = 8.3, 6.8 Hz, 1H), 6.74 – 6.58 (m, 3H), 4.88 (dd, *J* = 7.8, 6.3 Hz, 2H), 4.56 (t, *J* = 6.0 Hz, 2H), 4.17 (d, *J* = 6.7 Hz, 2H), 3.51 – 3.34 (m, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 163.6 (d, *J* = 245.3 Hz), 160.0 (d, *J* = 10.9 Hz), 130.2 (d, *J* = 10.1 Hz), 110.2 (d, *J* = 2.9 Hz), 107.8 (d, *J* = 21.3 Hz), 102.2 (d, *J* = 24.9 Hz), 74.1, 69.3, 34.4; **¹⁹F NMR (377 MHz, CDCl₃)** δ -111.50; **HRMS (ESI)** *calcd.* for (C₁₀H₁₂FO₂) [M+H]⁺ : 183.0816, *found* 183.0815.

3-((3-iodophenoxy)methyl)oxetane (S6):



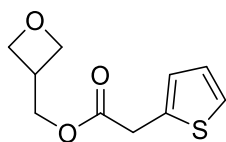
This compound was prepared according to **Method C** in 89% yield (258.1 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.26 – 7.16 (m, 2H), 6.92 (t, *J* = 8.0 Hz, 1H), 6.84 – 6.76 (m, 1H), 4.79 (dd, *J* = 7.8, 6.2 Hz, 2H), 4.47 (t, *J* = 6.1 Hz, 2H), 4.08 (d, *J* = 6.7 Hz, 2H), 3.40 – 3.27 (m, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 159.2, 130.8, 130.1, 123.6, 114.1, 94.3, 74.1, 69.1, 34.4; **HRMS (ESI)** *calcd.* for (C₁₀H₁₂IO₂) [M+H]⁺ : 290.9876, *found* 290.9882.

3-((naphthalen-1-yloxy)methyl)oxetane (S7):



This compound was prepared according to **Method C** in 87% yield (186.2 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.36 – 8.26 (m, 1H), 7.90 – 7.79 (m, 1H), 7.60 – 7.43 (m, 3H), 7.40 (dd, *J* = 8.3, 7.5 Hz, 1H), 6.85 (dd, *J* = 7.6, 1.0 Hz, 1H), 4.96 (dd, *J* = 7.9, 6.2 Hz, 2H), 4.73 (t, *J* = 6.1 Hz, 2H), 4.35 (d, *J* = 6.3 Hz, 2H), 3.73 – 3.49 (m, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 154.4, 134.5, 127.4, 126.5, 125.7, 125.5, 125.3, 121.8, 120.6, 104.7, 74.3, 68.9, 34.7; **HRMS (ESI)** *calcd.* for (C₁₄H₁₅O₂) [M+H]⁺ : 215.1067, *found* 215.1069.

oxetan-3-ylmethyl 2-(thiophen-2-yl)acetate (S8):

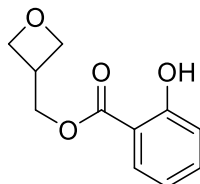


This compound was prepared according to **Method D** in 79% yield (167.5 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.29 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.18 – 7.12 (m, 1H), 7.03 (dd, *J* = 4.9, 1.3 Hz, 1H), 4.78 (dd, *J* = 7.9, 6.3 Hz, 2H), 4.45 (t, *J* = 6.2 Hz, 2H), 4.32 (d, *J* = 6.6 Hz, 2H), 3.68 (d, *J* = 0.9 Hz, 2H), 3.37 – 3.23 (m, 1H); **¹³C**

NMR (101 MHz, CDCl₃) δ 171.0, 133.3, 128.3, 125.8, 122.9, 73.9, 65.5, 35.7, 34.0;

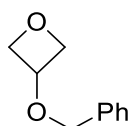
HRMS (ESI) *calcd.* for (C₁₀H₁₃O₃S) [M+H]⁺ : 213.0580, *found* 213.0583.

oxetan-3-ylmethyl 2-hydroxybenzoate (S9):



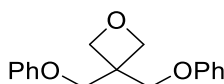
This compound was prepared according to **Method C** (NaHCO₃ as base) in 80% yield (166.4 mg) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 10.67 (s, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.41 (m, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.94 – 6.83 (m, 1H), 4.95 – 4.77 (m, 2H), 4.76 – 4.25 (m, 4H), 3.56 – 3.35 (m, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 170.0, 161.7, 136.0, 129.8, 119.2, 117.7, 112.1, 73.9, 65.8, 34.1; **HRMS (ESI)** *calcd.* for (C₁₁H₁₃O₄) [M+H]⁺ : 209.0808, *found* 209.0809.

3-(benzyloxy)oxetane (S10):



This compound was prepared according to **Method E** in 59% yield (96.8 mg) as yellow oil. It is a known compound with available analytical data¹.

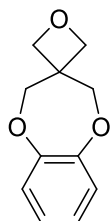
3,3-bis(phenoxymethyl)oxetane (S11):



This compound was prepared according to **Method F** in 95% yield (256.5 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.40 – 7.30 (m, 4H), 7.06 – 6.92 (m, 6H),

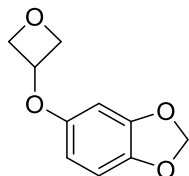
4.73 (s, 4H), 4.34 (s, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 158.7, 129.5, 121.1, 114.5, 75.8, 68.6, 43.4; HRMS (ESI) *calcd.* for $(\text{C}_{17}\text{H}_{19}\text{O}_3)$ $[\text{M}+\text{H}]^+$: 271.1329, *found* 271.1326.

2H,4H-spiro[benzo[b][1,4]dioxepine-3,3'-oxetane] (65):



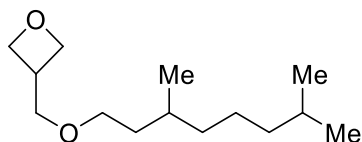
This compound was prepared according to **Method G** in 82% yield (157.4 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.12 – 6.80 (m, 4H), 4.58 (s, 4H), 4.40 (s, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 150.5, 123.7, 121.3, 77.1, 76.1, 44.8; HRMS (ESI) *calcd.* for $(\text{C}_{11}\text{H}_{13}\text{O}_3)$ $[\text{M}+\text{H}]^+$: 193.0859, *found* 193.0862.

5-(oxetan-3-yloxy)benzo[d][1,3]dioxole (S12):



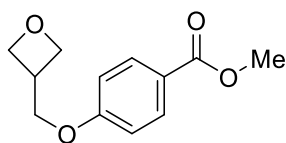
This compound was prepared according to **Method H** in 81% yield (157.1 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 6.67 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 2.5 Hz, 1H), 6.04 (dd, J = 8.4, 2.5 Hz, 1H), 5.91 (s, 2H), 5.10 (p, J = 5.6 Hz, 1H), 4.96 – 4.88 (m, 2H), 4.78 – 4.68 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 152.0, 148.5, 142.3, 108.0, 105.3, 101.3, 98.1, 78.0, 70.7; HRMS (ESI) *calcd.* for $(\text{C}_{10}\text{H}_{11}\text{O}_4)$ $[\text{M}+\text{H}]^+$: 195.0652, *found* 195.0653.

3-(((3,7-dimethyloctyl)oxy)methyl)oxetane (S13):



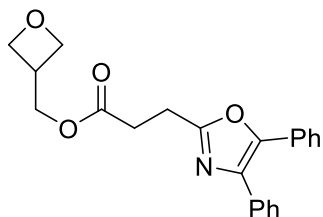
This compound was prepared according to **Method C** in 63% yield (143.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 4.79 (dd, *J* = 7.8, 6.1 Hz, 2H), 4.43 (t, *J* = 6.0 Hz, 2H), 3.65 (dd, *J* = 6.9, 1.1 Hz, 2H), 3.51 – 3.43 (m, 2H), 3.25 – 3.15 (m, 1H), 1.60 – 1.50 (m, 2H), 1.40 – 1.22 (m, 5H), 1.18 – 1.06 (m, 3H), 0.90 – 0.83 (m, 9H); **¹³C NMR (101 MHz, CDCl₃)** δ 74.8, 72.5, 69.7, 39.2, 37.3, 36.6, 35.0, 29.9, 27.9, 24.6, 22.7, 22.6, 19.6; **HRMS (ESI)** *calcd.* for (C₁₄H₂₉O₂) [M+H]⁺ : 229.2162, *found* 237.229.2163.

methyl 4-(oxetan-3-ylmethoxy)benzoate (S14):



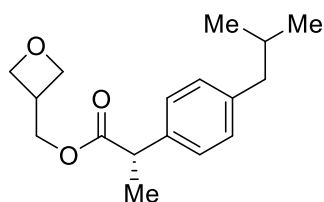
This compound was prepared according to **Method C** in 99% yield (219.8 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.02 – 7.94 (m, 2H), 6.95 – 6.88 (m, 2H), 4.93 – 4.82 (m, 2H), 4.56 (t, *J* = 6.0 Hz, 2H), 4.23 (d, *J* = 6.7 Hz, 2H), 3.87 (s, 3H), 3.44 (p, *J* = 7.0 Hz, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 166.7, 162.4, 131.6, 122.9, 114.0, 74.0, 69.1, 51.8, 34.4; **HRMS (ESI)** *calcd.* for (C₁₂H₁₅O₄) [M+H]⁺ : 223.0965, *found* 223.0963.

oxetan-3-ylmethyl 3-(4,5-diphenyloxazol-2-yl)propanoate (S15):



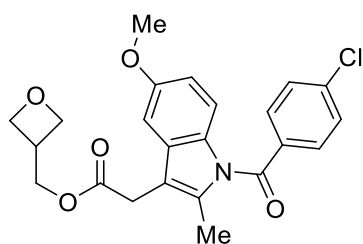
This compound was prepared according to **Method D** in 81% yield (294.0 mg) as yellow oil **¹H NMR (400 MHz, CDCl₃)** δ 7.71 – 7.60 (m, 2H), 7.57 (dd, J = 8.1, 1.7 Hz, 2H), 7.45 – 7.23 (m, 6H), 4.75 (dd, J = 7.9, 6.3 Hz, 2H), 4.45 (t, J = 6.1 Hz, 2H), 4.36 (d, J = 6.6 Hz, 2H), 3.27 (ddd, J = 14.3, 7.9, 6.3 Hz, 1H), 3.19 (t, J = 7.4 Hz, 2H), 2.94 (t, J = 7.4 Hz, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 171.9, 161.5, 145.4, 135.0, 132.3, 128.8, 128.6, 128.5, 128.4, 128.0, 127.8, 126.4, 73.9, 65.5, 33.9, 30.9, 23.4; **HRMS (ESI)** *calcd.* for (C₂₂H₂₂NO₄) [M+H]⁺ : 364.1543, *found* 364.1542.

oxetan-3-ylmethyl (S)-2-(4-isobutylphenyl)propanoate (S16):



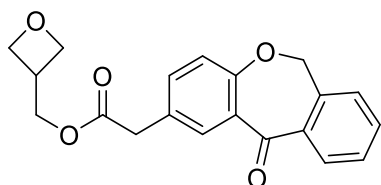
This compound was prepared according to **Method D** in 72% yield (198.7 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.22 – 7.16 (m, 2H), 7.13 – 7.06 (m, 2H), 4.94 – 4.50 (m, 2H), 4.42 – 4.33 (m, 2H), 4.27 (d, J = 6.6 Hz, 2H), 3.71 (q, J = 7.1 Hz, 1H), 3.36 – 2.98 (m, 1H), 2.44 (d, J = 7.2 Hz, 2H), 1.91 – 1.75 (m, 1H), 1.50 (d, J = 7.2 Hz, 3H), 0.89 (d, J = 6.6 Hz, 6H); **¹³C NMR (101 MHz, CDCl₃)** δ 174.7, 140.6, 137.5, 129.3, 127.0, 73.9, 65.2, 45.0(2), 44.9(6), 34.0, 30.1, 22.3, 18.2; **HRMS (ESI)** *calcd.* for (C₁₇H₂₅O₃) [M+H]⁺ : 277.1798, *found* 277.1800.

oxetan-3-ylmethyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (S17):



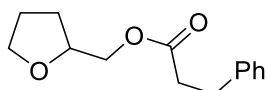
This compound was prepared according to **Method D** in 69% yield (294.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.70 – 7.63 (m, 2H), 7.50 – 7.44 (m, 2H), 6.94 (d, *J* = 2.5 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.74 (dd, *J* = 7.9, 6.2 Hz, 2H), 4.42 (t, *J* = 6.1 Hz, 2H), 4.32 (d, *J* = 6.4 Hz, 2H), 3.83 (s, 3H), 3.69 (s, 2H), 3.33 – 3.22 (m, 1H), 2.39 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 170.8, 168.3, 156.0, 139.3, 136.0, 133.8, 131.2, 130.8, 130.5, 129.1, 115.0, 112.3, 111.6, 101.3, 73.8, 65.5, 55.7, 34.0, 30.2, 13.3; **HRMS (ESI) *calcd.*** for (C₂₃H₂₃ClNO₅) [M+H]⁺ : 428.1259, *found* 428.1261.

oxetan-3-ylmethyl 2-(11-oxo-6,11-dihydrodibenzo[*b,e*]oxepin-2-yl)acetate (S18):



This compound was prepared according to **Method D** in 66% yield (223.1 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.10 (d, *J* = 2.4 Hz, 1H), 7.87 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.58 – 7.49 (m, 1H), 7.49 – 7.37 (m, 2H), 7.37 – 7.31 (m, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 5.16 (s, 2H), 4.76 (dd, *J* = 7.9, 6.3 Hz, 2H), 4.43 (t, *J* = 6.1 Hz, 2H), 4.32 (d, *J* = 6.7 Hz, 2H), 3.64 (s, 2H), 3.34 – 3.21 (m, 1H); **¹³C NMR (101 MHz, CDCl₃)** δ 190.7, 171.3, 160.4, 140.3, 136.1, 135.4, 132.7, 132.3, 129.4, 129.2, 127.7, 127.5, 125.1, 121.0, 73.9, 73.5, 65.6, 40.0, 33.9; **HRMS (ESI) *calcd.*** for (C₂₀H₁₉O₅) [M+H]⁺ : 339.1227, *found* 339.1230.

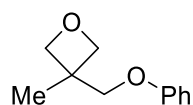
(tetrahydrofuran-2-yl)methyl 3-phenylpropanoate (S20):



This compound was prepared according to **Method D** in 50% yield (117.0 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.32 – 7.28 (m, 2H), 7.25 – 7.16 (m, 3H),

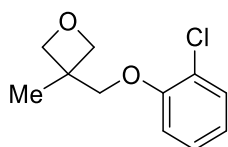
4.18 (dd, $J = 11.0, 3.4$ Hz, 1H), 4.15 – 4.07 (m, 1H), 4.07 – 3.99 (m, 1H), 3.93 – 3.85 (m, 1H), 3.85 – 3.76 (m, 1H), 2.98 (t, $J = 7.8$ Hz, 2H), 2.70 (t, $J = 7.8$ Hz, 2H), 2.03 – 1.84 (m, 3H), 1.62 – 1.51 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.7, 140.3, 128.4, 128.2, 126.1, 76.3, 68.3, 66.4, 35.6, 30.8, 27.8, 25.5; HRMS (ESI) *calcd.* for $(\text{C}_{14}\text{H}_{19}\text{O}_3)$ $[\text{M}+\text{H}]^+$: 235.1329, *found* 235.1331.

3-methyl-3-(phenoxymethyl)oxetane (S21):



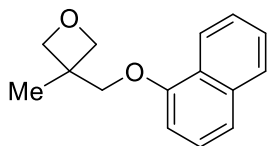
This compound was prepared according to **Method F** in 95% yield (169.1 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.40 – 7.27 (m, 2H), 7.12 – 6.87 (m, 3H), 4.67 (d, $J = 5.9$ Hz, 2H), 4.49 (d, $J = 5.9$ Hz, 2H), 4.05 (s, 2H), 1.48 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 158.9, 129.4, 120.9, 114.4, 79.7, 72.6, 39.6, 21.2; HRMS (ESI) *calcd.* for $(\text{C}_{11}\text{H}_{15}\text{O}_2)$ $[\text{M}+\text{H}]^+$: 179.1067, *found* 179.1069.

3-((2-chlorophenoxy)methyl)-3-methyloxetane (S22):



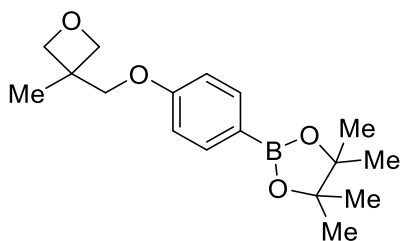
This compound was prepared according to **Method F** in 83% yield (176.0 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.36 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.26 – 7.16 (m, 1H), 7.00 – 6.86 (m, 2H), 4.66 (d, $J = 6.0$ Hz, 2H), 4.48 (d, $J = 6.0$ Hz, 2H), 4.08 (s, 2H), 1.48 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 154.4, 130.3, 127.6, 123.3, 121.7, 113.7, 79.7, 74.0, 39.9, 21.1; HRMS (ESI) *calcd.* for $(\text{C}_{11}\text{H}_{14}\text{ClO}_2)$ $[\text{M}+\text{H}]^+$: 213.0677, *found* 213.0681.

3-methyl-3-((naphthalen-1-yloxy)methyl)oxetane (S23):



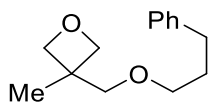
This compound was prepared according to **Method F** in 92% yield (209.8 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.40 – 8.27 (m, 1H), 7.92 – 7.78 (m, 1H), 7.61 – 7.47 (m, 3H), 7.47 – 7.38 (m, 1H), 6.93 – 6.79 (m, 1H), 4.80 (d, *J* = 5.9 Hz, 2H), 4.57 (d, *J* = 5.9 Hz, 2H), 4.17 (s, 2H), 1.56 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 154.5, 134.4, 127.4, 126.4, 125.7, 125.5, 125.2, 121.8, 120.4, 104.5, 79.7, 72.5, 39.7, 21.3; **HRMS (ESI)** *calcd.* for (C₁₅H₁₇O₂) [M+H]⁺ : 229.1223, *found* 229.1224.

4,4,5,5-tetramethyl-2-(4-((3-methyloxetan-3-yl)methoxy)phenyl)-1,3,2-dioxaborolane (S24):



This compound was prepared according to **Method F** in 89% yield (270.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.02 – 7.58 (m, 2H), 7.05 – 6.77 (m, 2H), 4.63 (d, *J* = 5.9 Hz, 2H), 4.45 (d, *J* = 5.9 Hz, 2H), 4.05 (s, 2H), 1.44 (s, 3H), 1.34 (s, 12H); **¹³C NMR (101 MHz, CDCl₃)** δ 161.6, 136.5, 113.9, 83.6, 79.8, 72.5, 39.6, 24.8, 21.3; **HRMS (ESI)** *calcd.* for (C₁₇H₂₆BO₄) [M+H]⁺ : 305.1919, *found* 305.1923.

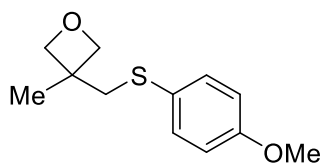
3-methyl-3-((3-phenylpropoxy)methyl)oxetane (S25):



This compound was prepared according to **Method I** in 88% yield (193.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.25 – 7.14 (m, 2H), 7.18 – 7.05 (m, 3H), 4.45 (d,

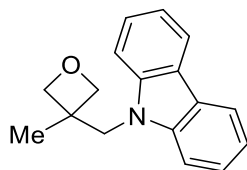
$J = 5.7$ Hz, 2H), 4.29 (d, $J = 5.7$ Hz, 2H), 3.43 – 3.34 (m, 4H), 2.68 – 2.53 (m, 2H), 1.89 – 1.74 (m, 2H), 1.25 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 141.9, 128.4, 128.3, 125.7, 80.2, 76.0, 70.4, 39.9, 32.3, 31.1, 21.4; HRMS (ESI) *calcd.* for ($\text{C}_{14}\text{H}_{21}\text{O}_2$) $[\text{M}+\text{H}]^+$: 221.1536, *found* 221.1540.

3-(((4-methoxyphenyl)thio)methyl)-3-methyloxetane (S26):



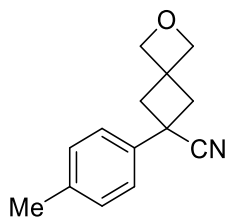
This compound was prepared according to **Method F** in 96% yield (215.0 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.44 – 7.33 (m, 2H), 6.93 – 6.78 (m, 2H), 4.42 (d, $J = 5.9$ Hz, 2H), 4.32 (d, $J = 5.9$ Hz, 2H), 3.79 (s, 3H), 3.18 (s, 2H), 1.40 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 159.1, 133.5, 126.7, 114.7, 81.9, 55.3, 45.9, 40.4, 23.2; HRMS (ESI) *calcd.* for ($\text{C}_{12}\text{H}_{17}\text{O}_2\text{S}$) $[\text{M}+\text{H}]^+$: 225.0944, *found* 225.0947.

9-((3-methyloxetan-3-yl)methyl)-9H-carbazole (S27):



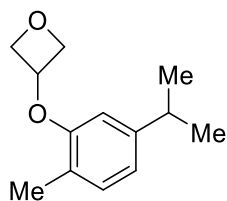
This compound was prepared according to **Method I** in 53% yield (133.0 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 8.20 – 8.05 (m, 2H), 7.55 – 7.46 (m, 2H), 7.47 – 7.39 (m, 2H), 7.37 – 7.14 (m, 2H), 4.81 (d, $J = 6.0$ Hz, 2H), 4.48 (s, 2H), 4.39 (d, $J = 5.9$ Hz, 2H), 1.49 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 141.2, 125.8, 123.0, 120.4, 119.3, 108.9, 80.7, 49.3, 43.0, 23.4; HRMS (ESI) *calcd.* for ($\text{C}_{17}\text{H}_{18}\text{NO}$) $[\text{M}+\text{H}]^+$: 252.1383, *found* 252.1387.

6-(*p*-tolyl)-2-oxaspiro[3.3]heptane-6-carbonitrile (S28):



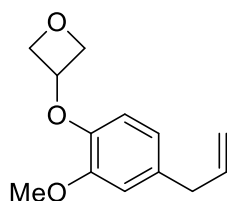
This compound was prepared according to **Method J** in 84% yield (178.9 mg) as yellow oil. It is a known compound with available analytical data².

3-(5-isopropyl-2-methylphenoxy)oxetane (S29):



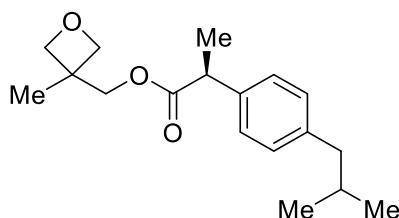
This compound was prepared according to **Method H** in 97% yield (199.8 mg) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.09 (d, *J* = 7.5 Hz, 1H), 6.78 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.21 (d, *J* = 1.7 Hz, 1H), 5.23 (p, *J* = 5.6 Hz, 1H), 4.99 (dd, *J* = 7.2, 6.0 Hz, 2H), 4.86 – 4.75 (m, 2H), 2.83 (p, *J* = 6.9 Hz, 1H), 2.23 (s, 3H), 1.22 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 154.7, 147.9, 130.9, 124.2, 118.8, 109.1, 78.3, 70.0, 34.0, 24.0, 15.8; HRMS (ESI) *calcd.* for (C₁₃H₁₉O₂) [M+H]⁺ : 207.1380, *found* 207.1381.

3-(4-allyl-2-methoxyphenoxy)oxetane (S30):



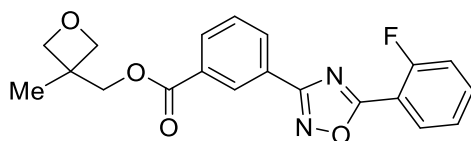
This compound was prepared according to **Method H** in 98% yield (215.6 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 6.74 (d, *J* = 2.0 Hz, 1H), 6.67 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.42 (d, *J* = 8.1 Hz, 1H), 6.02 – 5.87 (m, 1H), 5.17 (p, *J* = 5.8 Hz, 1H), 5.12 – 5.04 (m, 2H), 4.96 – 4.90 (m, 2H), 4.87 – 4.81 (m, 2H), 3.87 (s, 3H), 3.36 – 3.29 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 149.3, 144.4, 137.3, 134.1, 120.4, 115.8, 113.5, 112.5, 78.2, 71.3, 55.8, 39.7; **HRMS (ESI)** *calcd.* for (C₁₃H₁₇O₃) [M+H]⁺ : 221.1172, *found* 221.1173.

(3-methyloxetan-3-yl)methyl (S)-2-(4-isobutylphenyl)propanoate (S31):



This compound was prepared according to **Method F** in 94% yield (274.3 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.24 – 7.16 (m, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.42 (dd, *J* = 5.9, 3.0 Hz, 2H), 4.28 (dd, *J* = 5.9, 3.9 Hz, 2H), 4.20 – 4.06 (m, 2H), 3.74 (q, *J* = 7.2 Hz, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.91 – 1.76 (m, 1H), 1.52 (d, *J* = 7.2 Hz, 3H), 1.20 (s, 3H), 0.88 (d, *J* = 6.6 Hz, 6H); **¹³C NMR (101 MHz, CDCl₃)** δ 174.7, 140.6, 137.5, 129.3, 127.1, 79.4, 68.6, 45.1, 44.9, 39.2, 30.1, 22.3, 21.0, 18.0; **HRMS (ESI)** *calcd.* for (C₁₈H₂₇O₃) [M+H]⁺ : 291.1955, *found* 291.1959.

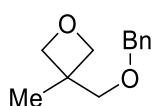
(3-methyloxetan-3-yl)methyl 3-(5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl)benzoate (S32):



This compound was prepared according to **Method F** in 49% yield (180.3 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.98 – 8.69 (m, 1H), 8.39 (dt, *J* = 7.8, 1.5

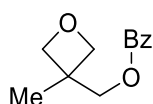
Hz, 1H), 8.28 – 8.16 (m, 2H), 7.67 – 7.54 (m, 2H), 7.46 – 7.26 (m, 2H), 4.66 (d, $J = 6.0$ Hz, 2H), 4.49 (d, $J = 6.4$ Hz, 4H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.1 (d, $J = 4.5$ Hz), 168.0, 165.8, 160.8 (d, $J = 260.8$ Hz), 134.7 (d, $J = 8.6$ Hz), 132.2, 132.0, 130.8 (d, $J = 17.0$ Hz), 129.1, 128.7, 127.4, 124.7 (d, $J = 3.7$ Hz), 117.3, 117.1, 112.7 (d, $J = 11.4$ Hz), 79.6, 69.4, 39.4, 21.3; ^{19}F NMR (377 MHz, CDCl_3) δ -108.14; HRMS (ESI) *calcd.* for $(\text{C}_{20}\text{H}_{18}\text{FN}_2\text{O}_4)$ $[\text{M}+\text{H}]^+$: 369.1245, *found* 369.1244.

3-((benzyloxy)methyl)-3-methyloxetane (S33):



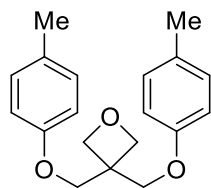
This compound was prepared according to **Method K** in 75% yield (144.0 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.64 – 6.93 (m, 5H), 4.58 (s, 2H), 4.53 (d, $J = 5.7$ Hz, 2H), 4.37 (d, $J = 5.7$ Hz, 2H), 3.53 (s, 2H), 1.34 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 138.3, 128.4, 127.6, 127.5, 80.1, 75.4, 73.3, 39.8, 21.4; HRMS (ESI) *calcd.* for $(\text{C}_{12}\text{H}_{17}\text{O}_2)$ $[\text{M}+\text{H}]^+$: 193.1223, *found* 193.1227.

(3-methyloxetan-3-yl)methyl benzoate (S34):



This compound was prepared according to **Method L** in 64% yield (131.8 mg) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 8.06 (dd, $J = 8.2, 1.1$ Hz, 2H), 7.60 – 7.54 (m, 1H), 7.45 (t, $J = 7.7$ Hz, 2H), 4.65 (d, $J = 5.7$ Hz, 2H), 4.46 (d, $J = 5.7$ Hz, 2H), 4.40 (s, 2H), 1.43 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 166.5, 133.1, 129.9, 129.6, 128.4, 79.6, 69.0, 39.3, 21.3; HRMS (ESI) *calcd.* for $(\text{C}_{12}\text{H}_{15}\text{O}_3)$ $[\text{M}+\text{H}]^+$: 207.1016, *found* 207.1019.

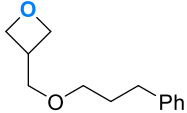
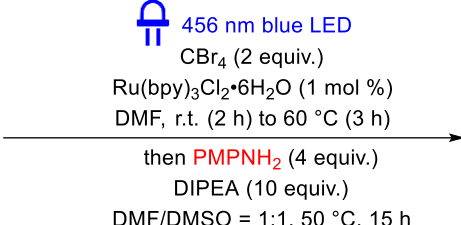
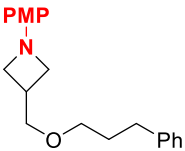
3,3-bis((*p*-tolyl)oxy)methyl)oxetane (S35):



This compound was prepared according to **Method F** in 90% yield (268.2 mg) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.09 (d, J = 8.4 Hz, 4H), 6.84 (d, J = 8.5 Hz, 4H), 4.68 (s, 4H), 4.27 (s, 4H), 2.29 (s, 6H); **¹³C NMR (101 MHz, CDCl₃)** δ 156.7, 130.4, 129.9, 114.4, 76.0, 69.0, 43.5, 20.4; **HRMS (ESI)** *calcd.* for (C₁₉H₂₃O₃) [M+H]⁺ : 299.1642, *found* 299.1643.

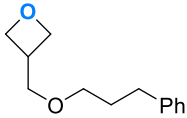
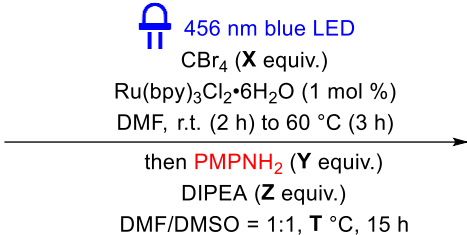
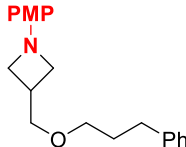
2. Supplementary Tables

Supplementary Table 1. Evaluation of reaction conditions.

 8   9		
Entry	Deviation from standard conditions	Yield [%]
1	none	85
2	no catalyst	<2
3	no light	<2
4	no heat	20
5	NBS instead of CBr ₄	<2
6	DBTCE instead of CBr ₄	<2
7	K ₂ CO ₃ instead of DIPEA	<2
8	Et ₃ N instead of DIPEA	32
9	NaH instead of DIPEA	<2
10	^t BuOK instead of DIPEA	<2
11	DBU instead of DIPEA	<2
12	THF instead of DMF/DMSO	<2
13	MeCN instead of DMF/DMSO	<2
14	DCM instead of DMF/DMSO	<2
15	Cyclohexane instead of DMF/DMSO	<2
16	DMSO instead of DMF/DMSO	<2
17	DMF instead of DMF/DMSO	65

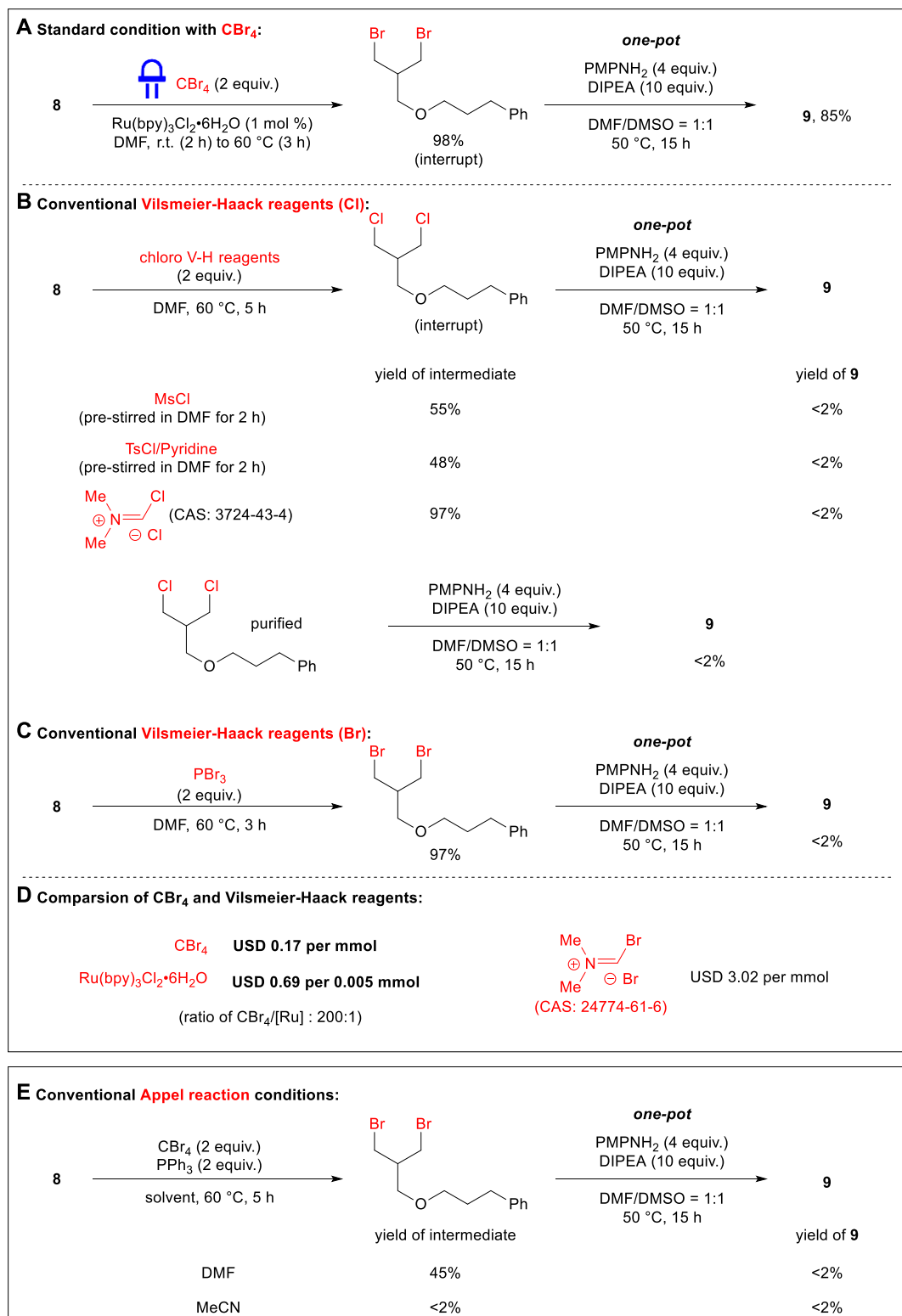
Standard reaction condition: mixture of oxetane **8** (0.05 mmol), CBr₄ (0.1 mmol), Ru(bpy)₃Cl₂·6H₂O (0.0005 mmol) and DMF (0.25 mL) was allowed to stir for 2 h at r.t., under 20 W blue LED, N₂ atmosphere. Then the mixture warmed to 60 °C and stirred for 3 h without blue LED, followed by addition of PMPNH₂ (0.2 mmol) and DIPEA (0.5 mmol) in DMSO (0.25 mL) and the reaction was allowed to stir for extra 15 h at 50 °C. Yields of **9** were determined by crude ¹H NMR with 1,3,5-trimethoxybenzene as internal standard.

Supplementary Table 2. Evaluation of reaction parameters.

 8   9					
Entry	CBr ₄ (X equiv.)	PMPNH ₂ (Y equiv.)	DIPEA (Z equiv.)	T °C	Yield [%]
1	1 equiv.	4 equiv.	10 equiv.	50 °C	61
2	3 equiv.	4 equiv.	10 equiv.	50 °C	82
3	2 equiv.	2 equiv.	10 equiv.	50 °C	34
4	2 equiv.	6 equiv.	10 equiv.	50 °C	71
5	2 equiv.	4 equiv.	5 equiv.	50 °C	65
6	2 equiv.	4 equiv.	8 equiv.	50 °C	74
7	2 equiv.	4 equiv.	10 equiv.	r.t.	20
8	2 equiv.	4 equiv.	10 equiv.	80 °C	75
9	2 equiv.	4 equiv.	10 equiv.	50 °C	85

General reaction condition: mixture of oxetane **8** (0.05 mmol), CBr₄, Ru(bpy)₃Cl₂·6H₂O (0.0005 mmol) and DMF (0.25 mL) was allowed to stir for 2 h at r.t., under 20 W blue LED, N₂ atmosphere. Then the mixture warmed to 60 °C and stirred for 3 h without blue LED, followed by addition of PMPNH₂ and DIPEA in DMSO (0.25 mL) and the reaction was allowed to stir for extra 15 h at r.t.-80 °C. Yields of **9** were determined by crude ¹H NMR with 1,3,5-trimethoxybenzene as internal standard.

Supplementary Table 3. Unsuccessful studies using Vilsmeier-Haack reagents and Appel reaction conditions.



A Standard conditions with CBr_4 and Ru catalyst providing dibromide intermediate or azetidine product. **B** Unsuccessful approach to azetidine with traditional chloro-Vilsmeier-Haack reagents. **C** Unsuccessful approach to azetidine with traditional bromo-Vilsmeier-Haack reagents. **D** Economical comparison of standard conditions with Vilsmeier-Haack reagent. **E** Unsuccessful approach to azetidine with traditional Appel reaction conditions.

3. Photocatalytic Oxygen-Atom Transmutation

Experimental procedures

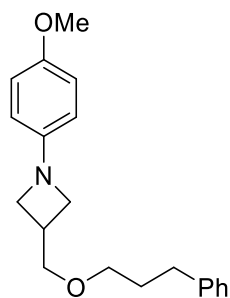
General procedure A: In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of amine (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15-46 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography.

General procedure B: In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography.

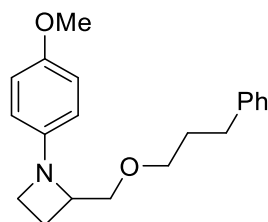
General procedure C: In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm)

illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.5 mmol, 5.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.2 mmol, 2.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 60 °C for 5 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography.

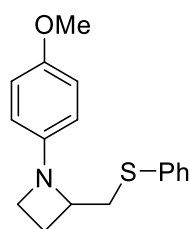
General procedure D: In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with ^tBuOK (0.6 mmol, 3.0 equiv.) and N-N/N-O source (0.3 mmol, 1.5 equiv.) in anhydrous DMF (1 mL), followed by addition of the above crude dibromide intermediate in anhydrous DMF (1 mL). The mixture was allowed to stir at 60 °C for 24 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography.



1-(4-methoxyphenyl)-3-((3-phenylpropoxy)methyl)azetidine (9): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH_2 (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **9** (52.9 mg, 85% yield) as yellow oil. **^1H NMR (400 MHz, CDCl_3)** δ 7.35 – 7.27 (m, 2H), 7.21 (dd, J = 7.4, 3.2 Hz, 3H), 6.90 – 6.80 (m, 2H), 6.53 – 6.35 (m, 2H), 3.92 (t, J = 7.4 Hz, 2H), 3.77 (s, 3H), 3.65 (d, J = 7.1 Hz, 2H), 3.58 (dd, J = 6.9, 5.4 Hz, 2H), 3.48 (t, J = 6.4 Hz, 2H), 3.03 – 2.88 (m, 1H), 2.78 – 2.66 (m, 2H), 1.97 – 1.88 (m, 2H); **^{13}C NMR (101 MHz, CDCl_3)** δ 152.1, 146.7, 141.8, 128.4, 128.3, 125.7, 114.6, 112.5, 73.3, 70.2, 55.8, 55.5, 32.2, 31.1, 30.1; **HRMS (ESI)** *calcd.* for $(\text{C}_{20}\text{H}_{26}\text{NO}_2)$ $[\text{M}+\text{H}]^+$: 312.1958, *found* 312.1963.

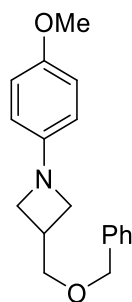


1-(4-methoxyphenyl)-2-((3-phenylpropoxy)methyl)azetidine (12): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 5 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **12** (33.6 mg, 54% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.33 – 7.26 (m, 2H), 7.19 (d, *J* = 6.9 Hz, 3H), 6.87 – 6.78 (m, 2H), 6.69 (d, *J* = 8.8 Hz, 2H), 4.20 – 4.05 (m, 1H), 4.03 – 3.90 (m, 1H), 3.75 (s, 4H), 3.66 – 3.46 (m, 4H), 2.78 – 2.65 (m, 2H), 2.37 – 2.15 (m, 2H), 2.00 – 1.88 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 152.5, 146.7, 142.0, 128.5, 128.3, 125.7, 124.3, 114.5, 113.7, 75.4, 70.7, 64.6, 55.8, 50.6, 32.4, 31.3, 20.5; **HRMS (ESI)** *calcd.* for (C₂₀H₂₆NO₂) [M+H]⁺ : 312.1958, *found* 312.1959.



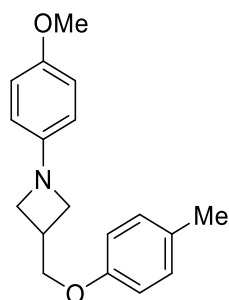
1-(4-methoxyphenyl)-2-((phenylthio)methyl)azetidine (13): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C

for 5 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 19 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **13** (31.9 mg, 56% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 7.44 – 7.41 (m, 2H), 7.34 – 7.29 (m, 2H), 7.26 – 7.22 (m, 1H), 6.86 – 6.82 (m, 2H), 6.52 (d, *J* = 8.4 Hz, 2H), 3.95 – 3.90 (m, 1H), 3.76 (s, 3H), 3.69 (t, *J* = 8.5 Hz, 1H), 3.46 – 3.40 (m, 1H), 3.37 – 3.31 (m, 1H), 3.26 (dd, *J* = 9.7, 5.6 Hz, 1H), 2.45 – 2.39 (m, 1H), 2.10 – 2.05 (m, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 151.2, 142.5, 135.4, 131.0, 129.0, 126.8, 115.0, 112.8, 55.9, 54.8, 47.3, 44.8, 32.2; **HRMS (ESI)** *calcd.* for (C₁₇H₂₀NOS) [M+H]⁺ : 286.1260, *found* 286.1260.

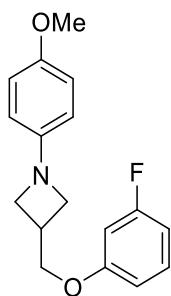


3-((benzyloxy)methyl)-1-(4-methoxyphenyl)azetidine (14): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **14** (39.6 mg, 70% yield) as yellow oil. **¹H NMR (600**

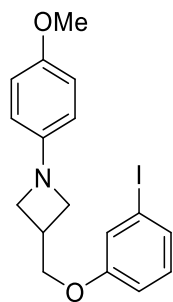
MHz, CDCl₃) δ 7.43 – 7.28 (m, 5H), 6.82 (d, J = 8.9 Hz, 2H), 6.43 (d, J = 8.8 Hz, 2H), 4.56 (s, 2H), 3.91 (t, J = 7.4 Hz, 2H), 3.75 (s, 3H), 3.69 (d, J = 7.0 Hz, 2H), 3.62 – 3.55 (m, 2H), 3.07 – 2.89 (m, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 152.1, 146.7, 138.2, 128.4, 127.7, 114.6, 112.6, 73.2, 72.7, 55.8, 55.5, 30.1; **HRMS (ESI)** *calcd.* for (C₁₈H₂₂NO₂) [M+H]⁺ : 284.1645, *found* 284.1647.



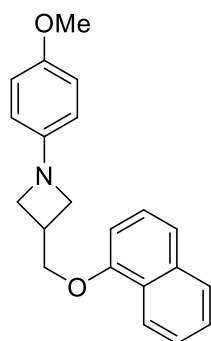
1-(4-methoxyphenyl)-3-((p-tolyloxy)methyl)azetidine (15): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **15** (40.8 mg, 72% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 7.09 (d, J = 8.4 Hz, 2H), 6.83 (dd, J = 10.6, 8.8 Hz, 4H), 6.48 (d, J = 8.6 Hz, 2H), 4.16 (d, J = 6.9 Hz, 2H), 4.00 (t, J = 7.3 Hz, 2H), 3.77 (s, 3H), 3.74 – 3.67 (m, 2H), 3.24 – 3.06 (m, 1H), 2.30 (s, 3H); **¹³C NMR (151 MHz, CDCl₃)** δ 156.7, 152.4, 146.4, 130.1, 129.9, 114.6, 114.4, 112.8, 70.0, 55.8, 55.4, 29.8, 20.4; **HRMS (ESI)** *calcd.* for (C₁₈H₂₂NO₂) [M+H]⁺ : 284.1645, *found* 284.1647.



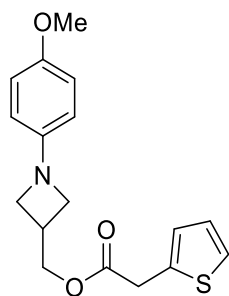
3-((3-fluorophenoxy)methyl)-1-(4-methoxyphenyl)azetidine (16): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **16** (42.5 mg, 74% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 7.23 (td, *J* = 8.3, 6.9 Hz, 1H), 6.87 – 6.80 (m, 2H), 6.73 – 6.61 (m, 3H), 6.51 – 6.42 (m, 2H), 4.18 (d, *J* = 6.9 Hz, 2H), 3.98 (t, *J* = 7.4 Hz, 2H), 3.76 (s, 3H), 3.69 (dd, *J* = 7.1, 5.2 Hz, 2H), 3.19 – 3.07 (m, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 163.6 (d, *J* = 245.2 Hz), 160.2 (d, *J* = 10.8 Hz), 152.3, 146.4, 130.2 (d, *J* = 10.0 Hz), 114.7, 112.7, 110.2 (d, *J* = 2.7 Hz), 107.7 (d, *J* = 21.3 Hz), 102.3 (d, *J* = 24.8 Hz), 70.2, 55.8, 55.2, 29.6; **¹⁹F NMR (377 MHz, CDCl₃)** δ -111.55; **HRMS (ESI)** *calcd.* for (C₁₇H₁₉FNO₂) [M+H]⁺ : 288.1394, *found* 288.1397.



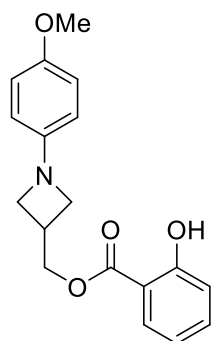
3-((3-iodophenoxy)methyl)-1-(4-methoxyphenyl)azetidine (17): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **17** (56.9 mg, 72% yield) as yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 7.32 – 7.26 (m, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.88 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.46 (d, *J* = 8.8 Hz, 2H), 4.16 (d, *J* = 6.9 Hz, 2H), 3.98 (t, *J* = 7.4 Hz, 2H), 3.76 (s, 3H), 3.71 – 3.64 (m, 2H), 3.19 – 3.06 (m, 1H); ¹³C NMR (151 MHz, CDCl₃) δ 159.3, 152.4, 146.3, 130.8, 130.1, 123.7, 114.7, 114.1, 112.8, 94.3, 70.0, 55.8, 55.2, 29.6; HRMS (ESI) *calcd.* for (C₁₇H₁₉INO₂) [M+H]⁺ : 396.0455, *found* 396.0456.



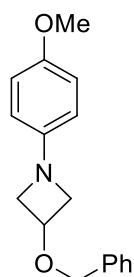
1-(4-methoxyphenyl)-3-((naphthalen-1-yloxy)methyl)azetidine (18): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:DCM = 1:1) to afford **18** (38.3 mg, 60% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 8.18 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.33 (m, 4H), 6.93 – 6.80 (m, 3H), 6.60 – 6.40 (m, 2H), 4.36 (d, *J* = 6.6 Hz, 2H), 4.08 (t, *J* = 7.5 Hz, 2H), 3.83 (dd, *J* = 7.0, 5.3 Hz, 2H), 3.78 (s, 3H), 3.37 – 3.23 (m, 1H); ¹³C NMR (101MHz, CDCl₃) δ 154.5, 152.3, 146.6, 134.5, 127.4, 126.4, 125.8, 125.6, 125.2, 121.9, 120.5, 114.7, 112.7, 104.7, 69.9, 55.8, 55.4, 29.9; HRMS (ESI) *calcd.* for (C₂₁H₂₂NO₂) [M+H]⁺ : 320.1645, *found* 320.1649.



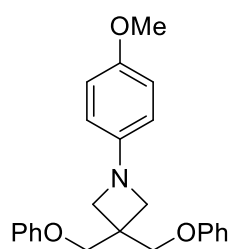
(1-(4-methoxyphenyl)azetidin-3-yl)methyl 2-(thiophen-2-yl)acetate (19): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH_2 (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:DCM = 1:1) to afford **19** (22.8 mg, 36% yield) as yellow oil. **^1H NMR (400 MHz, CDCl_3)** δ 7.28 – 7.22 (m, 1H), 7.16 – 7.09 (m, 1H), 7.01 (dd, J = 4.9, 1.1 Hz, 1H), 6.90 – 6.80 (m, 2H), 6.51 – 6.37 (m, 2H), 4.32 (d, J = 6.6 Hz, 2H), 3.89 (t, J = 7.5 Hz, 2H), 3.76 (s, 3H), 3.66 (s, 2H), 3.56 (dd, J = 7.0, 5.7 Hz, 2H), 3.07 – 2.92 (m, 1H); **^{13}C NMR (101MHz, CDCl_3)** δ 171.0, 152.4, 146.3, 133.4, 128.4, 125.8, 122.9, 114.7, 112.7, 66.2, 55.8, 55.0, 35.8, 29.2; **HRMS (ESI)** *calcd.* for $(\text{C}_{17}\text{H}_{20}\text{NO}_3\text{S})$ $[\text{M}+\text{H}]^+$: 318.1158, *found* 318.1161.



(1-(4-methoxyphenyl)azetidin-3-yl)methyl 2-hydroxybenzoate (20): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH_2 (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 17 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **20** (40.1 mg, 64% yield) as yellow oil. **^1H NMR (500 MHz, CDCl_3)** δ 10.70 (s, 1H), 7.77 (dd, J = 8.0, 1.8 Hz, 1H), 7.46 (ddd, J = 8.7, 7.2, 1.8 Hz, 1H), 6.98 (dd, J = 8.4, 1.2 Hz, 1H), 6.89 – 6.78 (m, 3H), 6.48 – 6.39 (m, 2H), 4.58 (d, J = 6.7 Hz, 2H), 3.99 (t, J = 7.5 Hz, 2H), 3.76 (s, 3H), 3.69 (dd, J = 7.2, 5.2 Hz, 2H), 3.20 – 3.07 (m, 1H); **^{13}C NMR (126 MHz, CDCl_3)** δ 170.0, 161.7, 152.5, 146.3, 135.9, 129.9, 119.2, 117.6, 114.7, 112.8, 112.2, 66.9, 55.8, 55.1, 29.2; **HRMS (ESI)** *calcd.* for ($\text{C}_{18}\text{H}_{20}\text{NO}_4$) $[\text{M}+\text{H}]^+$: 314.1387, *found* 314.1388.

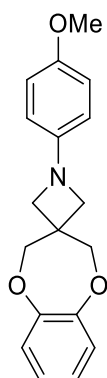


3-(benzyloxy)-1-(4-methoxyphenyl)azetidine (21): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:DCM = 1:1) to afford **21** (19.2 mg, 38% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.27 (m, 5H), 6.87 – 6.76 (m, 2H), 6.46 (d, *J* = 8.9 Hz, 2H), 4.51 (d, *J* = 3.8 Hz, 3H), 4.08 (t, *J* = 7.0 Hz, 2H), 3.75 (s, 3H), 3.66 (dd, *J* = 8.1, 5.1 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 152.6, 146.3, 137.5, 128.5, 127.9, 114.6, 113.3, 71.2, 68.3, 60.2, 55.8; HRMS (ESI) *calcd.* for (C₁₇H₂₀NO₂) [M+H]⁺ : 270.1489, *found* 270.1488.



1-(4-methoxyphenyl)-3,3-bis(phenoxy)methylazetidine (22): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL

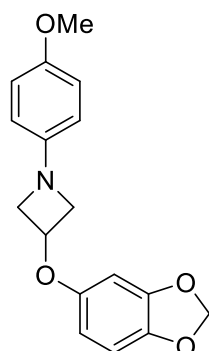
silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 2.0 mmol, 10.0 equiv.) in anhydrous DMF (0.5 mL). Then, PMPNH₂ (0.8 mmol, 4.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.5 mL). The mixture was allowed to stir at 60 °C for 12 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **22** (22.5 mg, 30% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 4H), 7.06 – 6.91 (m, 6H), 6.90 – 6.82 (m, 2H), 6.49 (d, *J* = 8.8 Hz, 2H), 4.33 (s, 4H), 3.86 (s, 4H), 3.78 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 158.9, 152.3, 146.2, 129.5, 121.0, 114.7, 114.6, 112.5, 69.4, 57.1, 55.8, 39.0; HRMS (ESI) *calcd.* for (C₂₄H₂₆NO₃) [M+H]⁺ : 376.1907, *found* 376.1913.



1-(4-methoxyphenyl)-2'*H*,4'*H*-spiro[azetidine-3,3'-benzo[*b*][1,4]dioxepine] (23**):**

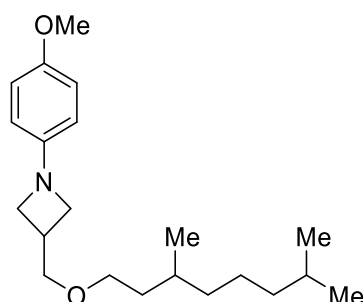
Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc =

10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 2.0 mmol, 10.0 equiv.) in anhydrous DMF (0.5 mL). Then, PMPNH₂ (0.8 mmol, 4.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.5 mL). The mixture was allowed to stir at 60 °C for 12 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **23** (20.8 mg, 35% yield) as white solid (m.p.: 135-137 °C). ¹H NMR (400 MHz, CDCl₃) δ 7.01 – 6.91 (m, 4H), 6.87 – 6.81 (m, 2H), 6.48 (d, *J* = 8.7 Hz, 2H), 4.36 (s, 4H), 3.77 (s, 3H), 3.74 (s, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 152.6, 150.7, 145.8, 123.6, 121.3, 114.8, 112.7, 58.4, 55.8, 40.3; HRMS (ESI) *calcd.* for (C₁₈H₂₀NO₃) [M+H]⁺ : 298.1438, *found* 298.1439.



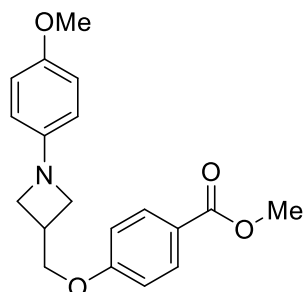
3-(benzo[d][1,3]dioxol-5-yloxy)-1-(4-methoxyphenyl)azetidine (24): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel,

hexanes:EtOAc = 10:1) to afford **24** (20.9 mg, 35% yield) as yellow oil. **¹H NMR (500 MHz, CDCl₃)** δ 6.86 – 6.80 (m, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.49 (d, *J* = 8.8 Hz, 2H), 6.42 (d, *J* = 2.5 Hz, 1H), 6.19 (dd, *J* = 8.4, 2.5 Hz, 1H), 5.93 (s, 2H), 5.03 – 4.93 (m, 1H), 4.35 – 4.22 (m, 2H), 3.81 (dd, *J* = 8.3, 4.6 Hz, 2H), 3.76 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 152.7, 152.2, 148.5, 145.8, 142.2, 114.7, 113.2, 108.0, 105.7, 101.3, 98.2, 67.2, 59.8, 55.8; **HRMS (ESI)** *calcd.* for (C₁₇H₁₈NO₄) [M+H]⁺ : 300.1230, *found* 300.1230.

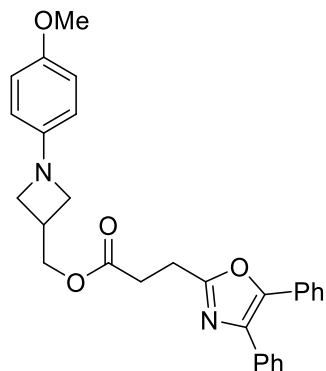


3-(((3,7-dimethyloctyl)oxy)methyl)-1-(4-methoxyphenyl)azetidine (25): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **25** (44.6 mg, 67% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 6.87 – 6.76 (m, 2H), 6.43 (d, *J* = 8.8 Hz, 2H), 3.90 (t, *J* = 7.4 Hz, 2H), 3.75 (s, 3H), 3.63 (dd, *J* = 7.1, 2.0 Hz, 2H), 3.58 – 3.53 (m, 2H), 3.52 – 3.44 (m, 2H), 3.00 – 2.84 (m, 1H), 1.65 – 1.58 (m, 1H), 1.56 – 1.48 (m, 2H), 1.41 – 1.35 (m, 1H), 1.30 – 1.24 (m, 3H), 1.17 – 1.08 (m, 3H), 0.90 – 0.86 (m,

9H); ^{13}C NMR (126 MHz, CDCl_3) δ 152.1, 146.8, 114.6, 112.5, 73.4, 69.7, 55.8, 55.6, 39.3, 37.3, 36.6, 30.1, 29.9, 27.9, 24.6, 22.7, 22.6, 19.7; HRMS (ESI) *calcd.* for $(\text{C}_{21}\text{H}_{36}\text{NO}_2)$ $[\text{M}+\text{H}]^+$: 334.2741, *found* 334.2748.

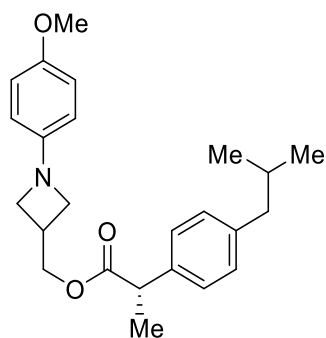


methyl 4-((1-(4-methoxyphenyl)azetidin-3-yl)methoxy)benzoate (26): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH_2 (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **26** (49.1 mg, 75% yield) as yellow oil. ^1H NMR (500 MHz, CDCl_3) δ 7.99 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.9 Hz, 2H), 6.86 – 6.80 (m, 2H), 6.46 (d, J = 8.8 Hz, 2H), 4.25 (d, J = 6.9 Hz, 2H), 3.99 (t, J = 7.4 Hz, 2H), 3.89 (s, 3H), 3.76 (s, 3H), 3.70 (dd, J = 7.0, 5.3 Hz, 2H), 3.24 – 3.08 (m, 1H); ^{13}C NMR (151 MHz, CDCl_3) δ 166.8, 162.5, 152.4, 146.3, 131.6, 122.8, 114.7, 114.1, 112.7, 70.0, 55.8, 55.2, 51.9, 29.6; HRMS (ESI) *calcd.* for $(\text{C}_{19}\text{H}_{22}\text{NO}_4)$ $[\text{M}+\text{H}]^+$: 328.1543, *found* 328.1547.



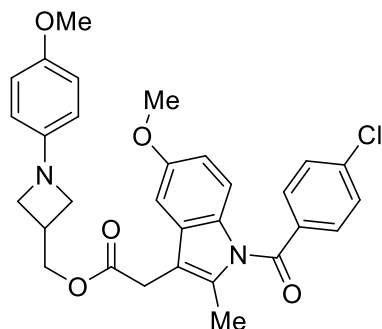
(1-(4-methoxyphenyl)azetidin-3-yl)methyl 3-(4,5-diphenyloxazol-2-yl)propanoate

(27): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 43 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **27** (36.5 mg, 39% yield) as yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.67 – 7.61 (m, 2H), 7.61 – 7.55 (m, 2H), 7.42 – 7.29 (m, 6H), 6.84 – 6.73 (m, 2H), 6.36 (d, *J* = 8.9 Hz, 2H), 4.36 (d, *J* = 7.0 Hz, 2H), 3.86 (t, *J* = 7.4 Hz, 2H), 3.74 (s, 3H), 3.55 (dd, *J* = 6.9, 5.5 Hz, 2H), 3.18 (t, *J* = 7.4 Hz, 2H), 3.02 – 2.89 (m, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 171.9, 161.6, 152.3, 146.3, 145.4, 135.1, 132.4, 128.9, 128.6, 128.5(4), 128.4(6), 128.1, 127.8, 126.4, 114.6, 112.6, 66.5, 55.8, 55.0, 31.0, 29.2, 23.5; HRMS (ESI) *calcd.* for (C₂₉H₂₉N₂O₄) [M+H]⁺ : 469.2122, *found* 469.2121.

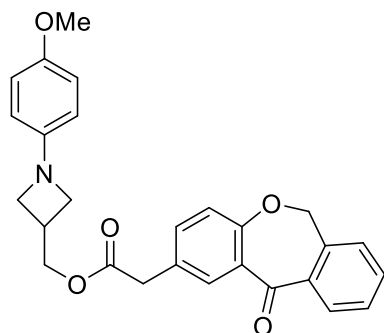


(1-(4-methoxyphenyl)azetidin-3-yl)methyl (S)-2-(4-isobutylphenyl)propanoate

(28): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 16 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **28** (48.0 mg, 63% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 7.17 (d, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.85 – 6.77 (m, 2H), 6.38 (d, *J* = 8.7 Hz, 2H), 4.33 – 4.18 (m, 2H), 3.81 (q, *J* = 7.7 Hz, 2H), 3.76 (s, 3H), 3.69 (q, *J* = 7.1 Hz, 1H), 3.48 (t, *J* = 6.2 Hz, 2H), 3.03 – 2.84 (m, 1H), 2.45 (d, *J* = 7.2 Hz, 2H), 1.89 – 1.81 (m, 1H), 1.48 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 6H); **¹³C NMR (151 MHz, CDCl₃)** δ 174.7, 152.3, 146.4, 140.5, 137.6, 129.3, 127.1, 114.6, 112.6, 66.0, 55.8, 54.9, 45.1, 45.0, 30.2, 29.2, 22.4, 18.2; **HRMS (ESI)** *calcd.* for (C₂₄H₃₂NO₃) [M+H]⁺ : 382.2377, *found* 382.2376.



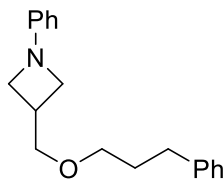
(1-(4-methoxyphenyl)azetidin-3-yl)methyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (29): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 44 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **29** (40.4 mg, 38% yield) as yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 2.4 Hz, 1H), 6.86 (d, *J* = 9.0 Hz, 1H), 6.82 – 6.77 (m, 2H), 6.67 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.38 (d, *J* = 8.7 Hz, 2H), 4.32 (d, *J* = 6.6 Hz, 2H), 3.86 (t, *J* = 7.4 Hz, 2H), 3.83 (s, 3H), 3.74 (s, 3H), 3.67 (s, 2H), 3.55 – 3.49 (m, 2H), 3.05 – 2.91 (m, 1H), 2.35 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 170.8, 168.2, 156.0, 152.4, 146.1, 139.2, 135.9, 133.8, 131.1, 130.8, 130.5, 129.1, 115.0, 114.6, 112.7, 112.4, 111.5, 101.3, 66.3, 55.7(4), 55.6(9), 55.0, 30.3, 29.2, 13.3; HRMS (ESI) *calcd.* for (C₃₀H₃₀ClN₂O₅) [M+H]⁺ : 533.1838, *found* 533.1839.



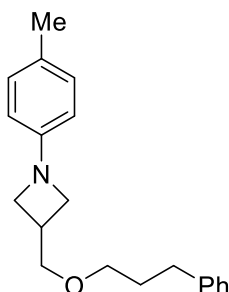
(1-(4-methoxyphenyl)azetidin-3-yl)methyl

2-(11-oxo-6,11-

dihydrodibenzo[b,e]oxepin-2-yl)acetate (30): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PMPNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 46 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **30** (39.0 mg, 44% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 8.11 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.56 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (td, *J* = 7.6, 1.3 Hz, 1H), 7.43 – 7.35 (m, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.86 – 6.78 (m, 2H), 6.43 (d, *J* = 8.3 Hz, 2H), 5.18 (s, 2H), 4.33 (d, *J* = 6.7 Hz, 2H), 3.90 (t, *J* = 7.5 Hz, 2H), 3.74 (s, 3H), 3.65 (s, 2H), 3.57 (dd, *J* = 7.2, 5.5 Hz, 2H), 3.07 – 2.95 (m, 1H); **¹³C NMR (151 MHz, CDCl₃)** δ 190.8, 171.3, 160.5, 152.5, 146.0, 140.4, 136.3, 135.5, 132.8, 132.4, 129.5, 129.3, 127.9, 127.6, 125.1, 121.1, 114.7, 112.9, 73.2, 66.3, 55.8, 55.1, 40.2, 29.2; **HRMS (ESI) *calcd.*** for (C₂₇H₂₆NO₅) [M+H]⁺ : 444.1805, *found* 444.1808.

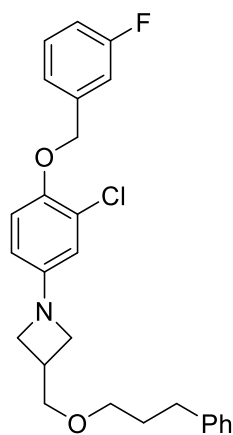


1-phenyl-3-((3-phenylpropoxy)methyl)azetidine (31): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of PhNH_2 (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **31** (30.9 mg, 55% yield) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.36 – 6.95 (m, 7H), 6.67 (t, J = 7.3 Hz, 1H), 6.41 (d, J = 7.7 Hz, 2H), 3.91 (t, J = 7.5 Hz, 2H), 3.56 (t, J = 6.9 Hz, 4H), 3.39 (t, J = 6.4 Hz, 2H), 2.91 (dq, J = 12.9, 6.6, 5.8 Hz, 1H), 2.72 – 2.57 (m, 2H), 1.91 – 1.77 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 151.6, 141.8, 128.9, 128.4, 128.3, 125.8, 117.7, 111.6, 73.1, 70.3, 55.1, 32.3, 31.1, 30.1; HRMS (ESI) *calcd.* for $(\text{C}_{19}\text{H}_{24}\text{NO})$ $[\text{M}+\text{H}]^+$: 282.1852, *found* 282.1856.



3-((3-phenylpropoxy)methyl)-1-(p-tolyl)azetidine (32): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4

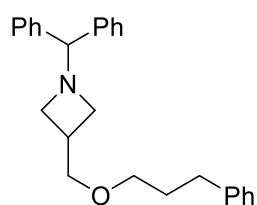
mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of *p*-toluidine (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **32** (43.7 mg, 74% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.35 – 7.28 (m, 2H), 7.24 – 7.13 (m, 3H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.44 (d, *J* = 8.4 Hz, 2H), 3.97 (t, *J* = 7.5 Hz, 2H), 3.75 – 3.54 (m, 4H), 3.49 (t, *J* = 6.4 Hz, 2H), 3.07 – 2.91 (m, 1H), 2.78 – 2.65 (m, 2H), 2.28 (s, 3H), 2.00 – 1.86 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 149.8, 141.9, 129.4, 128.4, 128.3, 125.8, 111.7, 73.2, 70.3, 55.4, 32.2, 31.1, 30.1, 20.4; **HRMS (ESI)** *calcd.* for (C₂₀H₂₆NO) [M+H]⁺ : 296.2009, *found* 296.2015.



1-(3-chloro-4-((3-fluorobenzyl)oxy)phenyl)-3-((3-

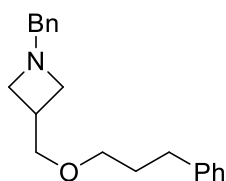
phenylpropoxy)methyl)azetidine (33): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room

temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of 3-chloro-4-((3-fluorobenzyl)oxy)aniline (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **33** (59.7 mg, 68% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.39 – 7.26 (m, 3H), 7.25 – 7.16 (m, 5H), 7.06 – 6.96 (m, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.53 (d, *J* = 2.7 Hz, 1H), 6.29 (dd, *J* = 8.7, 2.8 Hz, 1H), 5.04 (s, 2H), 3.93 (t, *J* = 7.5 Hz, 2H), 3.68 – 3.57 (m, 4H), 3.48 (t, *J* = 6.4 Hz, 2H), 3.05 – 2.88 (m, 1H), 2.74 – 2.67 (m, 2H), 1.97 – 1.88 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 162.9 (d, *J* = 245.8 Hz), 147.6, 146.1, 141.8, 139.8 (d, *J* = 7.4 Hz), 130.0 (d, *J* = 8.2 Hz), 128.4, 128.3, 125.8, 124.7, 122.6 (d, *J* = 2.9 Hz), 116.9, 114.6 (d, *J* = 21.1 Hz), 114.1 (d, *J* = 22.0 Hz), 113.5, 110.5, 72.9, 71.6, 70.3, 55.3, 32.2, 31.1, 30.0; **¹⁹F NMR (377 MHz, CDCl₃)** δ -112.88; **HRMS (ESI)** *calcd.* for (C₂₆H₂₈ClFNO₂) [M+H]⁺ : 440.1787, *found* 440.1787.



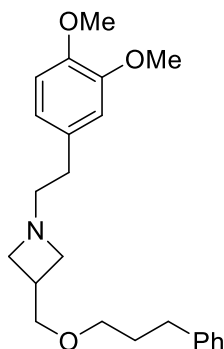
1-benzhydryl-3-((3-phenylpropoxy)methyl)azetidine (34): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the

solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, benzhydramine (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 12 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **34** (32.7 mg, 44% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.42 – 7.39 (m, 4H), 7.30 – 7.24 (m, 6H), 7.20 – 7.14 (m, 5H), 4.37 (s, 1H), 3.54 (d, *J* = 6.6 Hz, 2H), 3.41 (t, *J* = 6.4 Hz, 2H), 3.32 (t, *J* = 7.6 Hz, 2H), 2.92 (t, *J* = 6.9 Hz, 2H), 2.74 – 2.65 (m, 3H), 1.91 – 1.85 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 142.1, 141.9, 128.4(3), 128.3(8), 128.3, 127.5, 127.0, 125.7, 78.0, 73.2, 70.1, 56.6, 32.3, 31.2, 29.8; **HRMS (ESI)** *calcd.* for (C₂₆H₃₀NO) [M+H]⁺ : 372.2322, *found* 372.2325.



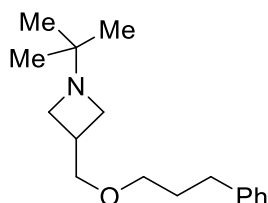
1-benzyl-3-((3-phenylpropoxy)methyl)azetidine (35): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, BnNH₂ (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 17 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1, with 5% Et₃N) to afford **35** (38.7 mg, 65% yield) as yellow oil.

¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.13 (m, 7H), 7.13 – 7.04 (m, 3H), 3.52 (s, 2H), 3.45 (d, *J* = 6.6 Hz, 2H), 3.37 – 3.28 (m, 4H), 2.92 (t, *J* = 6.8 Hz, 2H), 2.72 – 2.56 (m, 3H), 1.84 – 1.75 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 141.9, 138.1, 128.4(1), 128.3(9), 128.2, 126.9, 125.7, 73.0, 70.1, 63.5, 57.3, 32.2, 31.2, 30.7; **HRMS (ESI)** *calcd.* for (C₂₀H₂₆NO) [M+H]⁺ : 296.2009, *found* 296.2011.

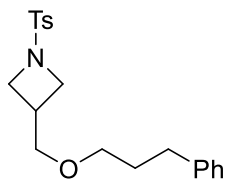


1-(3,4-dimethoxyphenethyl)-3-((3-phenylpropoxy)methyl)azetidine (36): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, 2-(3,4-dimethoxyphenyl)ethanamine (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1, with 5% Et₃N) to afford **36** (62.0 mg, 84% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.32 – 7.28 (m, 2H), 7.21 (dd, *J* = 7.2, 3.2 Hz, 3H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.77 – 6.73 (m, 2H), 3.88 (d, *J* = 6.1 Hz, 6H), 3.55 (d, *J* = 6.7 Hz, 2H), 3.50 – 3.36 (m, 4H), 2.98 (dd, *J* = 7.4, 6.1 Hz, 2H), 2.77 – 2.66 (m, 5H), 2.65 – 2.56 (m, 2H), 1.96 – 1.87 (m, 2H); **¹³C NMR (101**

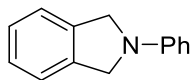
MHz, CDCl₃) δ 148.8, 147.3, 141.9, 132.7, 128.4, 128.3, 125.7, 120.5, 112.0, 111.2, 73.1, 70.2, 61.6, 57.6, 55.9, 55.8, 34.0, 32.3, 31.2, 30.8; **HRMS (ESI)** *calcd.* for (C₂₃H₃₂NO₃) [M+H]⁺ : 370.2377, *found* 370.2379.



1-(*tert*-butyl)-3-((3-phenylpropoxy)methyl)azetidine (37): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, *tert*-butylamine (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1, with 5% Et₃N) to afford **37** (19.4 mg, 37% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.23 – 7.18 (m, 2H), 7.16 – 7.07 (m, 3H), 3.41 (d, *J* = 6.5 Hz, 2H), 3.35 (t, *J* = 6.4 Hz, 2H), 3.23 (t, *J* = 7.6 Hz, 2H), 2.97 (dd, *J* = 7.4, 6.6 Hz, 2H), 2.61 (dd, *J* = 8.6, 6.7 Hz, 3H), 1.85 – 1.78 (m, 2H), 0.88 (s, 9H); **¹³C NMR (101 MHz, CDCl₃)** δ 142.0, 128.4, 128.3, 125.7, 73.0, 70.1, 51.9, 49.3, 32.3, 31.3, 28.4, 24.0; **HRMS (ESI)** *calcd.* for (C₁₇H₂₈NO) [M+H]⁺ : 262.2165, *found* 262.2168.

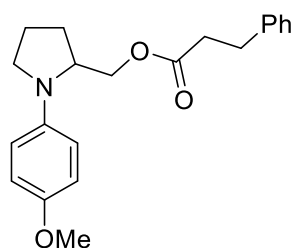


3-((3-phenylpropoxy)methyl)-1-tosylazetidine (38): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of TsNH₂ (0.8 mmol, 4.0 equiv.) and K₂CO₃ (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 50 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **38** (22.2 mg, 31% yield) as yellow oil. ¹H NMR (500 MHz, CDCl₃) δ 7.79 – 7.66 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.31 – 7.26 (m, 2H), 7.22 – 7.11 (m, 3H), 3.83 (t, *J* = 8.1 Hz, 2H), 3.56 (dd, *J* = 8.0, 6.0 Hz, 2H), 3.36 – 3.26 (m, 4H), 2.68 – 2.55 (m, 3H), 2.40 (s, 3H), 1.80 – 1.69 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 143.9, 141.7, 131.6, 129.7, 128.4(0), 128.3(7), 128.3, 125.9, 71.2, 70.2, 53.1, 32.1, 30.9, 28.4, 21.5; HRMS (ESI) *calcd.* for (C₂₀H₂₆NO₃S) [M+H]⁺ : 360.1628, *found* 360.1632.



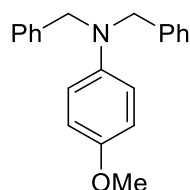
2-phenylisoindoline (39): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.), LiBr (10.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue

LED was turned off and the mixture was allowed to stir at 100 °C for 20 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in toluene (1 mL). Then, PhNH₂ (0.4 mmol, 2.0 equiv.) and DIPEA (1.0 mmol, 5.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 60 °C for 4 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **39** (16.1 mg, 41% yield) as yellow oil. It is a known compound with available analytical data³.

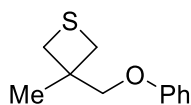


(1-(4-methoxyphenyl)pyrrolidin-2-yl)methyl 3-phenylpropanoate (40): Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.8 mmol, 4.0 equiv.), LiBr (10.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 80 °C for 24 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (1 mL). Then, PMPNH₂ (0.4 mmol, 2.0 equiv.) and DIPEA (1.0 mmol, 5.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 60 °C for 19 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **40** (21.7 mg, 32% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.27 (m, 2H), 7.26 – 7.14

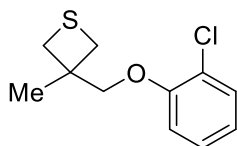
(m, 3H), 6.93 – 6.83 (m, 2H), 6.68 (d, $J = 8.0$ Hz, 2H), 4.31 (dd, $J = 10.3, 3.1$ Hz, 1H), 3.93 – 3.78 (m, 2H), 3.77 (s, 3H), 3.57 – 3.34 (m, 1H), 3.08 (q, $J = 8.4$ Hz, 1H), 2.97 (t, $J = 7.8$ Hz, 2H), 2.66 (t, $J = 7.8$ Hz, 2H), 2.14 – 1.79 (m, 4H); ^{13}C NMR (151 MHz, CDCl_3) δ 172.9, 151.2, 142.2, 140.4, 128.5, 128.3, 126.3, 115.0, 112.9, 64.5, 57.4, 55.9, 49.2, 35.8, 30.9, 28.6, 23.3; HRMS (ESI) *calcd.* for $(\text{C}_{21}\text{H}_{26}\text{NO}_3)$ $[\text{M}+\text{H}]^+$: 340.1907, *found* 340.1910.



***N,N*-dibenzyl-4-methoxyaniline (42):** Based on the general procedure A, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 42 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL). Then, PMPNH_2 (0.1 mmol, 0.5 equiv.) and DIPEA (0.5 mmol, 2.5 equiv) was added in one portion. Then, the mixture was allowed to stir at room temperature for 3 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **42** (24.2 mg, 40% yield) as yellow oil. It is a known compound with available analytical data⁴.

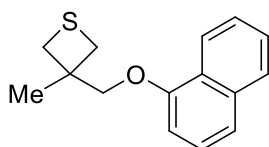


3-methyl-3-(phenoxymethyl)thietane (43): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **43** (17.9 mg, 92% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H), 7.00 – 6.90 (m, 3H), 3.94 (s, 2H), 3.21 (d, *J* = 9.2 Hz, 2H), 2.96 (d, *J* = 9.2 Hz, 2H), 1.43 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 159.1, 129.5, 120.9, 114.5, 74.1, 44.2, 33.5, 25.2; HRMS (ESI) *calcd.* for (C₁₁H₁₅OS) [M+H]⁺ : 195.0838, *found* 195.0844.



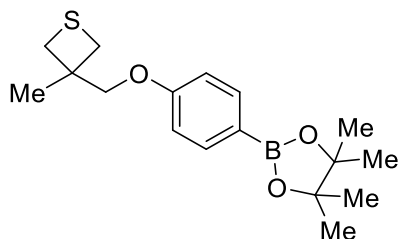
3-((2-chlorophenoxy)methyl)-3-methylthietane (44): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by

evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **44** (22.3 mg, 98% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.36 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.26 – 7.15 (m, 1H), 6.96 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.95 – 6.87 (m, 1H), 4.01 (s, 2H), 3.22 (d, *J* = 9.3 Hz, 2H), 3.00 (d, *J* = 9.3 Hz, 2H), 1.47 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 154.5, 130.3, 127.7, 123.3, 121.6, 113.7, 75.3, 44.4, 33.5, 25.2; **HRMS (ESI) *calcd.*** for (C₁₁H₁₄ClOS) [M+H]⁺ : 229.0448, *found* 229.0449.



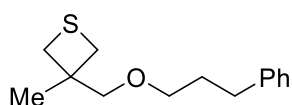
3-methyl-3-((naphthalen-1-yloxy)methyl)thietane (45): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **45** (20.3 mg, 83% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.40 – 8.24 (m, 1H), 7.93 – 7.73 (m, 1H), 7.62 – 7.43 (m, 3H), 7.39 (t, *J* = 7.9 Hz, 1H), 6.85 (d, *J* = 7.5 Hz, 1H), 4.11 (s, 2H), 3.36 (d, *J* = 9.2 Hz, 2H), 3.05 (d, *J* = 9.2 Hz, 2H), 1.55 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 154.6, 134.5, 127.5, 126.5, 125.8, 125.6, 125.3, 121.9, 120.5, 104.6,

74.3, 44.4, 33.6, 25.4; **HRMS (ESI)** *calcd.* for (C₁₅H₁₇OS) [M+H]⁺ : 245.0995, *found* 245.1000.

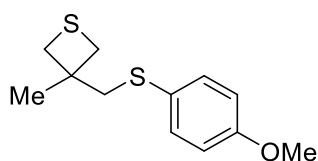


4,4,5,5-tetramethyl-2-((3-methylthietan-3-yl)methoxy)phenyl-1,3,2-

dioxaborolane (46): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **46** (19.2 mg, 60% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.76 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 3.96 (s, 2H), 3.20 (d, *J* = 9.2 Hz, 2H), 2.95 (d, *J* = 9.2 Hz, 2H), 1.42 (s, 3H), 1.34 (s, 12H); **¹³C NMR (101 MHz, CDCl₃)** δ 161.7, 136.5, 113.9, 83.6, 74.0, 44.2, 33.5, 25.2, 24.8; **HRMS (ESI)** *calcd.* for (C₁₇H₂₆BO₃S) [M+H]⁺ : 321.1690, *found* 321.1689.

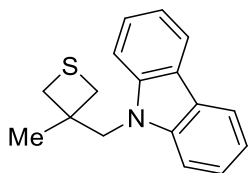


3-methyl-3-((3-phenylpropoxy)methyl)thietane (47): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **47** (21.5 mg, 91% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.27 (m, 2H), 7.20 (d, *J* = 7.1 Hz, 3H), 3.48 (t, *J* = 6.3 Hz, 2H), 3.37 (s, 2H), 3.12 (d, *J* = 9.0 Hz, 2H), 2.84 (d, *J* = 9.0 Hz, 2H), 2.74 – 2.69 (m, 2H), 1.98 – 1.86 (m, 2H), 1.33 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 141.9, 128.4, 128.3, 125.7, 77.6, 70.4, 44.5, 33.7, 32.3, 31.1, 25.3; HRMS (ESI) *calcd.* for (C₁₄H₂₁OS) [M+H]⁺ : 237.1308, *found* 237.1313.



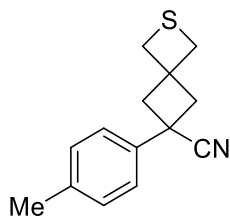
3-(((4-methoxyphenyl)thio)methyl)-3-methylthietane (48): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C

for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **48** (14.4 mg, 60% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.53 – 7.29 (m, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.37 – 3.04 (m, 4H), 2.87 (d, *J* = 8.2 Hz, 2H), 1.38 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 158.9, 133.1, 127.2, 114.7, 55.3, 48.4, 45.0, 36.2, 26.8; **HRMS (ESI) *calcd.* for (C₁₂H₁₇OS₂) [M+H]⁺ : 241.0715, *found* 241.0719.**

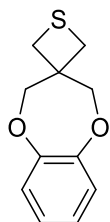


9-((3-methylthietan-3-yl)methyl)-9H-carbazole (49): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **49** (25.3 mg, 95% yield) as white solid (m.p.: 102-104 °C). **¹H NMR (400 MHz, CDCl₃)** δ 8.01 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.32 (m, 2H), 7.17 – 7.12 (m, 2H), 4.38

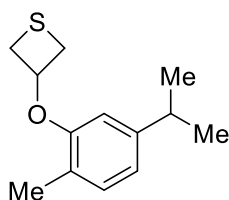
(s, 2H), 3.16 (d, $J = 9.3$ Hz, 2H), 2.88 (d, $J = 9.4$ Hz, 2H), 1.37 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 141.7, 125.7, 123.0, 120.2, 119.3, 109.3, 51.5, 48.4, 35.5, 27.6; HRMS (ESI) *calcd.* for ($\text{C}_{17}\text{H}_{18}\text{NS}$) $[\text{M}+\text{H}]^+$: 268.1154, *found* 268.1156.



6-(*p*-tolyl)-2-thiaspiro[3.3]heptane-6-carbonitrile (50): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr_4 (0.2 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 24 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 5:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 60 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **50** (13.7 mg, 60% yield) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.26 – 7.09 (m, 4H), 3.56 (s, 2H), 3.16 (s, 2H), 3.12 – 3.04 (m, 2H), 2.73 – 2.64 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 138.0, 136.0, 129.7, 125.5, 124.2, 48.3, 43.6, 39.2, 38.0, 34.2, 21.0; HRMS (ESI) *calcd.* for ($\text{C}_{14}\text{H}_{16}\text{NS}$) $[\text{M}+\text{H}]^+$: 230.0998, *found* 230.0995.

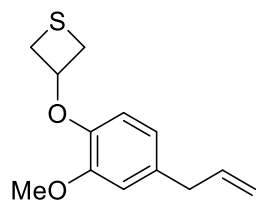


2H,4H-spiro[benzo[b][1,4]dioxepine-3,3'-thietane] (51): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 h. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **51** (18.0 mg, 87% yield) as white solid (m.p.: 83-85 °C). ¹H NMR (400 MHz, CDCl₃) δ 6.96 – 6.80 (m, 4H), 4.15 (s, 4H), 3.00 (s, 4H); ¹³C NMR (101 MHz, CDCl₃) δ 150.9, 123.7, 121.5, 77.7, 48.2, 29.8; HRMS (ESI) *calcd.* for (C₁₁H₁₃O₂S) [M+H]⁺ : 209.0631, *found* 209.0633.



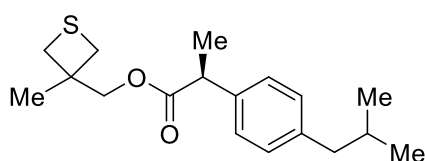
3-(5-isopropyl-2-methylphenoxy)thietane (52): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction

vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 60 °C for 15 min. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **52** (16.1 mg, 73% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.07 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.55 (s, 1H), 5.31 (p, *J* = 7.7 Hz, 1H), 3.65 – 3.56 (m, 2H), 3.45 – 3.37 (m, 2H), 2.89 – 2.81 (m, 1H), 2.18 (s, 3H), 1.23 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 154.5, 147.9, 130.9, 124.4, 119.1, 110.5, 71.6, 36.1, 34.0, 24.1, 15.8; HRMS (ESI) *calcd.* for (C₁₃H₁₉OS) [M+H]⁺ : 223.1151, *found* 223.1155.



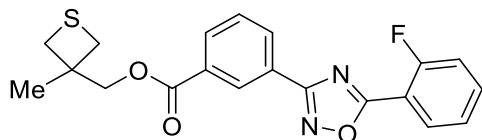
3-(4-allyl-2-methoxyphenoxy)thietane (53): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 60 °C for

15 min. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **53** (7.6 mg, 32% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 6.77 – 6.63 (m, 3H), 6.05 – 5.83 (m, 1H), 5.24 (p, *J* = 7.8 Hz, 1H), 5.13 – 5.03 (m, 2H), 3.85 (s, 3H), 3.70 – 3.59 (m, 2H), 3.40 – 3.29 (m, 4H); **¹³C NMR (101 MHz, CDCl₃)** δ 149.6, 143.9, 137.4, 134.4, 120.4, 115.8, 115.2, 112.6, 72.6, 55.8, 39.8, 36.0; **HRMS (ESI) *calcd.*** for (C₁₃H₁₇O₂S) [M+H]⁺ : 237.0944, *found* 237.0949.



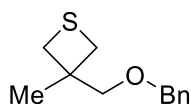
(3-methylthietan-3-yl)methyl (S)-2-(4-isobutylphenyl)propanoate (54): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **54** (15.3 mg, 50% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.21 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.08 (d, *J* = 10.9 Hz, 1H), 4.00 (d, *J* = 10.9 Hz, 1H), 3.74 (q, *J* = 7.2 Hz, 1H), 2.98 (t, *J* = 8.2 Hz, 2H), 2.76 (dd, *J* = 8.9, 6.2 Hz, 2H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.91 – 1.76 (m, 1H), 1.53 (d, *J* = 7.2 Hz, 3H), 1.19 (s, 3H), 0.88 (d, *J* = 6.6 Hz, 6H); **¹³C NMR (101 MHz, CDCl₃)** δ 174.7, 140.6, 137.5,

129.3, 127.2, 70.2, 45.2, 45.0, 43.6, 33.2, 30.2, 24.8, 22.3, 18.0; **HRMS (ESI)** *calcd.* for (C₁₈H₂₇O₂S) [M+H]⁺ : 307.1726, *found* 307.1730.

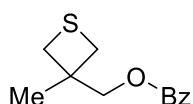


(3-methylthietan-3-yl)methyl 3-(5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl)benzoate

(55): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 2:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **55** (12.3 mg, 32% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.87 (t, *J* = 1.5 Hz, 1H), 8.39 (dt, *J* = 7.8, 1.4 Hz, 1H), 8.29 – 8.19 (m, 2H), 7.67 – 7.59 (m, 2H), 7.39 – 7.27 (m, 2H), 4.39 (s, 2H), 3.24 (d, *J* = 9.3 Hz, 2H), 3.00 (d, *J* = 9.3 Hz, 2H), 1.45 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 173.1, 168.0, 165.8, 160.8 (d, *J* = 261.0 Hz), 134.7 (d, *J* = 8.7 Hz), 132.1 (d, *J* = 21.6 Hz), 131.0, 130.9, 129.2, 128.8, 127.4, 124.7 (d, *J* = 3.9 Hz), 117.2 (d, *J* = 20.9 Hz), 112.7 (d, *J* = 11.4 Hz), 71.0, 43.7, 33.4, 25.2; **¹⁹F NMR (377 MHz, CDCl₃)** δ -108.13; **HRMS (ESI)** *calcd.* for (C₂₀H₁₈FN₂O₃S) [M+H]⁺ : 385.1017, *found* 385.1020.

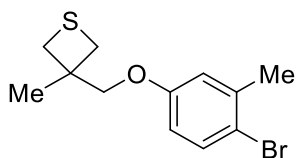


3-((benzyloxy)methyl)-3-methylthietane (56): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **56** (14.3 mg, 69% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 5H), 4.58 (s, 2H), 3.42 (s, 2H), 3.13 (d, *J* = 9.0 Hz, 2H), 2.83 (d, *J* = 9.0 Hz, 2H), 1.33 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 128.4, 127.6, 127.5, 77.1, 73.3, 44.5, 33.7, 25.3; HRMS (ESI) *calcd.* for (C₁₂H₁₇OS) [M+H]⁺ : 209.0995, *found* 209.0996.



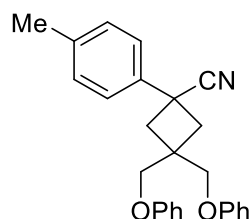
(3-methylthietan-3-yl)methyl benzoate (57): Based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol,

4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **57** (17.3 mg, 78% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.25 – 7.95 (m, 2H), 7.65 – 7.55 (m, 1H), 7.52 – 7.38 (m, 2H), 4.31 (s, 2H), 3.22 (d, *J* = 9.2 Hz, 2H), 2.95 (d, *J* = 9.2 Hz, 2H), 1.42 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 166.5, 133.1, 130.0, 129.6, 128.4, 70.7, 43.7, 33.4, 25.1; **HRMS (ESI)** *calcd.* for (C₁₂H₁₅O₂S) [M+H]⁺ : 223.0787, *found* 223.0790.



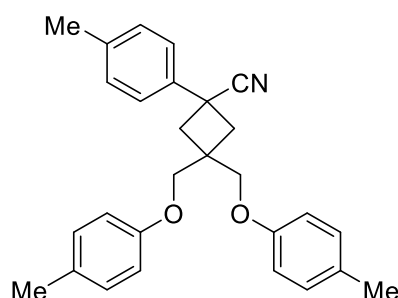
3-((4-bromo-3-methylphenoxy)methyl)-3-methylthietane (59): To a solution of commercially available 3-(bromomethyl)-3-methyloxetane (0.2 mmol, 1.0 equiv.) and 4-bromo-3-methylphenol (0.2 mmol, 1.0 equiv.) in dried MeCN, Cs₂CO₃ (0.4 mmol, 2.0 equiv.) was added in one portion at room temperature. The mixture was allowed to stir overnight under 80 °C. After completion of the reaction, the reaction was quenched with saturated solution of NH₄Cl. The mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The resulting crude product was purified by column chromatography (silica gel, hexanes:EtOAc = 10:1) to afford the desired 3-((4-bromo-3-methylphenoxy)methyl)-3-methyloxetane. Then, based on the general procedure B, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL

solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **59** (16.1 mg, 53% yield overall) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.40 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 2.9 Hz, 1H), 6.65 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.89 (s, 2H), 3.17 (d, *J* = 9.2 Hz, 2H), 2.95 (d, *J* = 9.3 Hz, 2H), 2.37 (s, 3H), 1.41 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 158.3, 138.9, 132.8, 117.2, 115.6, 113.5, 74.3, 44.2, 33.5, 25.2, 23.1; HRMS (ESI) *calcd.* for (C₁₂H₁₆BrOS) [M+H]⁺ : 287.0100, *found* 287.0105.



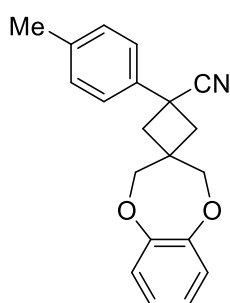
3,3-bis(phenoxy)methyl-1-(p-tolyl)cyclobutane-1-carbonitrile (60): Based on the general procedure C, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.5 mmol, 5.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.2 mmol, 2.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 60 °C for 5 hours. After completion of the reaction, the

crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **60** (25.8 mg, 67% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.48 (d, J = 8.2 Hz, 2H), 7.36 – 7.25 (m, 6H), 7.06 – 6.94 (m, 4H), 6.92 – 6.85 (m, 2H), 4.38 (s, 2H), 4.03 (s, 2H), 2.98 (q, J = 13.6 Hz, 4H), 2.40 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 158.7, 158.6, 137.8, 137.1, 129.6, 129.5(4), 129.5(2), 125.7, 124.9, 121.2(0), 121.1(6), 114.6, 114.4, 70.5, 38.7, 37.7, 33.4, 21.0; **HRMS (ESI) calcd.** for (C₂₆H₂₆NO₂) [M+H]⁺ : 384.1958, *found* 384.1961.



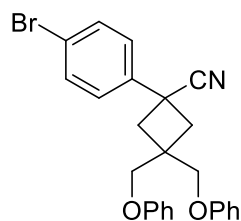
1-(*p*-tolyl)-3,3-bis((*p*-tolyloxy)methyl)cyclobutane-1-carbonitrile (61**):** Based on the general procedure C, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.5 mmol, 5.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.2 mmol, 2.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 60 °C for 5 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc =

10:1) to afford **61** (20.1 mg, 49% yield) as white solid (m.p.: 105-107 °C). **¹H NMR (400 MHz, CDCl₃)** δ 7.38 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 7.3 Hz, 2H), 7.00 (dd, *J* = 17.3, 8.3 Hz, 4H), 6.86 – 6.79 (m, 2H), 6.73 – 6.62 (m, 2H), 4.24 (s, 2H), 3.89 (s, 2H), 2.85 (q, *J* = 13.5 Hz, 4H), 2.29 (s, 3H), 2.22 (s, 3H), 2.20 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 156.7, 156.6, 137.7, 137.2, 130.3(9), 130.3(7), 129.9(4), 129.9(2), 129.6, 125.8, 124.9, 114.5, 114.3, 70.8(1), 70.7(7), 38.7, 37.8, 33.4, 21.0, 20.5, 20.4; **HRMS (ESI) calcd.** for (C₂₈H₃₀NO₂) [M+H]⁺ : 412.2271, *found* 412.2273.



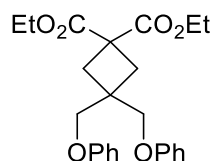
3'-(*p*-tolyl)-2*H*,4*H*-spiro[benzo[*b*][1,4]dioxepine-3,1'-cyclobutane]-3'-carbonitrile (62**):** Based on the general procedure C, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.5 mmol, 5.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.2 mmol, 2.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 60 °C for 5 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography

(silica gel, hexanes:EtOAc = 10:1) to afford **62** (28.3 mg, 93% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.37 – 7.31 (m, 2H), 7.29 – 7.25 (m, 2H), 7.07 – 7.01 (m, 1H), 7.01 – 6.89 (m, 3H), 4.48 (s, 2H), 4.05 (s, 2H), 3.02 – 2.91 (m, 2H), 2.74 – 2.60 (m, 2H), 2.40 (s, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 150.8, 150.6, 138.1, 136.6, 129.8, 125.6, 124.3, 123.7, 123.6, 121.4, 121.2, 78.6, 77.7, 40.0, 38.9, 33.2, 21.0; **HRMS (ESI)** *calcd.* for (C₂₀H₂₀NO₂) [M+H]⁺ : 306.1489, *found* 306.1491.

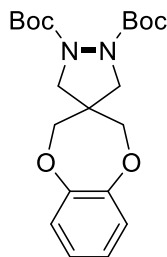


1-(4-bromophenyl)-3,3-bis(phenoxy)methylcyclobutane-1-carbonitrile (63): Based on the general procedure C, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.5 mmol, 5.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.2 mmol, 2.0 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 60 °C for 5 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **63** (30.2 mg, 68% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.63 – 7.56 (m, 2H), 7.52 – 7.46 (m, 2H), 7.38 – 7.26 (m, 4H), 7.07 – 6.95 (m, 4H), 6.92 – 6.79 (m, 2H), 4.36 (s, 2H), 4.02 (s, 2H), 2.99 (q, *J* = 13.6 Hz, 4H); **¹³C NMR**

(101 MHz, CDCl₃) δ 158.6, 158.5, 139.1, 132.1, 129.5(9), 129.5(7), 127.7, 124.2, 122.1, 121.3, 114.6, 114.4, 70.6, 70.4, 38.5, 37.8, 33.3; HRMS (ESI) *calcd.* for (C₂₅H₂₂BrNNaO₂) [M+Na]⁺ : 470.0726, *found* 470.0727.

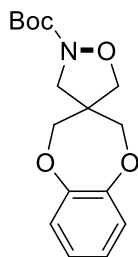


diethyl 3,3-bis(phenoxymethyl)cyclobutane-1,1-dicarboxylate (64): Based on the general procedure C, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with NaH (60 % dispersion in mineral oil, 0.4 mmol, 4.0 equiv.) in anhydrous DMF (0.25 mL). Then, carbon source (0.42 mmol, 4.2 equiv.) was added in one portion, followed by addition of the above crude dibromide intermediate in anhydrous DMF (0.25 mL). The mixture was allowed to stir at 120 °C for 20 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **64** (17.8 mg, 43% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.28 (dd, *J* = 8.6, 7.4 Hz, 4H), 7.01 – 6.86 (m, 6H), 4.25 (q, *J* = 7.1 Hz, 4H), 4.08 (s, 4H), 2.71 (s, 4H), 1.27 (t, *J* = 7.1 Hz, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 171.8, 159.0, 129.4, 120.9, 114.6, 70.4, 61.6, 47.3, 36.7, 33.2, 14.0; HRMS (ESI) *calcd.* for (C₂₄H₂₉O₆) [M+H]⁺ : 413.1959, *found* 413.1962.



di-tert-butyl 2H,4H-spiro[benzo[b][1,4]dioxepine-3,4'-pyrazolidine]-1',2'-

dicarboxylate (66): Based on the general procedure D, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with ^tBuOK (0.6 mmol, 3.0 equiv.) and di-tert-butyl hydrazine-1,2-dicarboxylate (0.3 mmol, 1.5 equiv.) in anhydrous DMF (1 mL), followed by addition of the above crude dibromide intermediate in anhydrous DMF (1 mL). The mixture was allowed to stir at 60 °C for 24 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography. (silica gel, hexanes:EtOAc = 5:1) to afford **66** (38.1 mg, 47% yield) as white solid (m.p.: 119-121 °C). **¹H NMR (400 MHz, CDCl₃)** δ 7.01 – 6.87 (m, 4H), 4.01 (d, *J* = 14.7 Hz, 6H), 3.18 (d, *J* = 9.3 Hz, 2H), 1.50 (s, 18H); **¹³C NMR (101 MHz, CDCl₃)** δ 155.6, 150.7, 123.8, 121.3, 81.7, 75.6, 52.7, 51.7, 28.2; **HRMS (ESI)** *calcd.* for (C₂₁H₃₀N₂NaO₆) [M+Na]⁺ : 429.1996, *found* 429.1993.

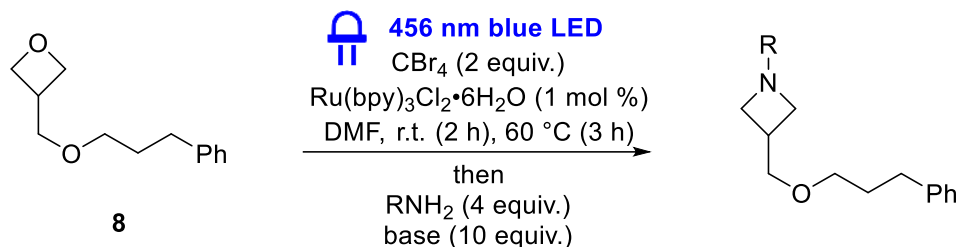


***tert*-butyl 2*H*,4*H*-spiro[benzo[*b*][1,4]dioxepine-3,4'-isoxazolidine]-2'-carboxylate**

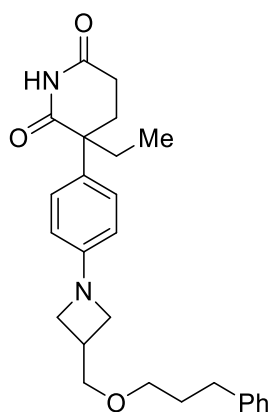
(67): Based on the general procedure D, in a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 90 °C for 20 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with *t*BuOK (0.6 mmol, 3.0 equiv.) and *tert*-butyl hydroxycarbamate (0.3 mmol, 1.5 equiv.) in anhydrous DMF (1 mL), followed by addition of the above crude dibromide intermediate in anhydrous DMF (1 mL). The mixture was allowed to stir at 60 °C for 24 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography. (silica gel, hexanes:EtOAc = 5:1) to afford **67** (33.1 mg, 54% yield) as white solid (m.p.: 143-145 °C). ¹H NMR (400 MHz, CDCl₃) δ 7.10 – 6.73 (m, 4H), 4.17 (d, *J* = 12.2 Hz, 2H), 4.09 (d, *J* = 12.1 Hz, 2H), 3.92 (s, 2H), 3.58 (s, 2H), 1.52 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 157.3, 150.6, 123.8, 121.3, 82.6, 75.5, 74.4, 54.1, 54.0, 28.1; HRMS (ESI) *calcd.* for (C₁₆H₂₁NNaO₅) [M+Na]⁺ : 330.1312, *found* 330.1314.

4. Late-Stage Editing and Applications

Late-stage editing with densely functionalized bioactive amines



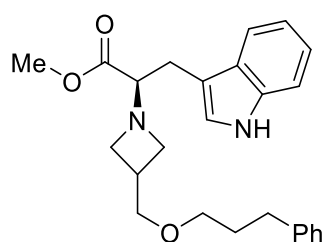
Functionalized bioactive amines aminoglutethimide, *L*-Phe methyl ester, *D*-Trp methyl ester, mexiletine and oseltamivir are commercially available (Sigma-Aldrich and BLD pharm).



3-ethyl-3-(4-(3-((3-phenylpropoxy)methyl)azetidin-1-yl)phenyl)piperidine-2,6-

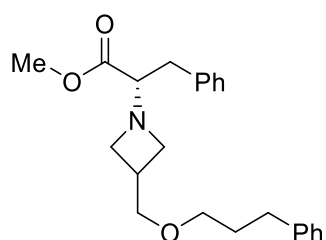
dione (68): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, a solution of aminoglutethimide (0.8 mmol, 4.0 equiv.) and DIPEA (2.0 mmol, 10.0 equiv) in DMSO (1 mL) was added in one portion. Then, the mixture was allowed to stir at 60 °C for 48 hours. After

completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1) to afford **68** (64.7 mg, 77% yield) as yellow oil. **¹H NMR (600 MHz, CDCl₃)** δ 8.20 (s, 1H), 7.30 – 7.26 (m, 2H), 7.22 – 7.16 (m, 3H), 7.14 – 7.07 (m, 2H), 6.52 – 6.35 (m, 2H), 3.97 (t, J = 7.5 Hz, 2H), 3.69 – 3.58 (m, 4H), 3.47 (t, J = 6.4 Hz, 2H), 3.07 – 2.87 (m, 1H), 2.73 – 2.65 (m, 2H), 2.61 – 2.52 (m, 1H), 2.50 – 2.39 (m, 1H), 2.35 – 2.25 (m, 1H), 2.16 (td, J = 13.8, 4.5 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.94 – 1.85 (m, 3H), 0.85 (t, J = 7.4 Hz, 3H); **¹³C NMR (151 MHz, CDCl₃)** δ 175.6, 172.7, 150.7, 141.8, 128.4, 128.3, 126.9, 126.7, 125.8, 111.7, 73.1, 70.3, 54.9, 50.2, 32.9, 32.2, 31.1, 30.0, 29.3, 26.9, 9.0; **HRMS (ESI)** *calcd.* for (C₂₆H₃₃N₂O₃) [M+H]⁺ : 421.2486, *found* 421.2489.



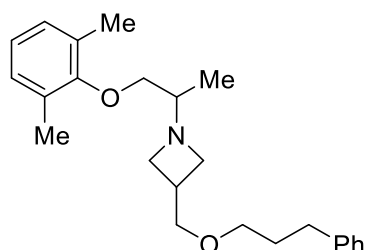
methyl (R)-3-(1H-indol-3-yl)-2-(3-((3-phenylpropoxy)methyl)azetidin-1-yl)propanoate (69): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, *D*-Trp methyl ester (0.8 mmol, 4.0 equiv.) and Na₂CO₃ (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1, with 5% Et₃N) to afford **69** (46.1 mg, 57% yield) as

yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.09 (s, 1H), 7.51 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.26 – 7.16 (m, 3H), 7.13 – 7.08 (m, 3H), 7.07 – 6.99 (m, 1H), 6.94 (d, *J* = 2.4 Hz, 1H), 3.50 (s, 3H), 3.50 – 3.38 (m, 4H), 3.38 – 3.28 (m, 3H), 3.13 – 2.89 (m, 4H), 2.74 (s, 1H), 2.60 (dd, *J* = 8.6, 6.7 Hz, 2H), 1.85 – 1.78 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 172.6, 141.9, 136.1, 128.4, 128.3, 127.4, 125.7, 122.7, 121.9, 119.3, 118.6, 111.2, 111.1, 72.8, 70.6, 70.2, 56.0, 55.9, 51.6, 32.3, 31.2, 30.6, 26.1; **HRMS (ESI) *calcd.* for (C₂₅H₃₁N₂O₃) [M+H]⁺ : 407.2329, *found* 407.2331.**



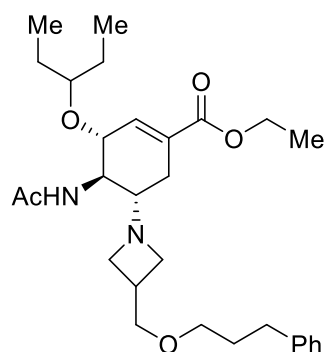
methyl (S)-3-phenyl-2-(3-((3-phenylpropoxy)methyl)azetidin-1-yl)propanoate (82): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, *L*-Phe methyl ester (0.8 mmol, 4.0 equiv.) and Na₂CO₃ (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1, with 5% Et₃N) to afford **82** (32.1 mg, 44% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.29 – 7.25 (m, 4H), 7.24 – 7.12 (m, 6H), 3.61 (s, 3H), 3.54 – 3.40 (m, 6H), 3.32 (t, *J* = 7.0 Hz, 1H), 3.15 – 3.00 (m, 2H), 2.92 – 2.82 (m, 2H), 2.82 – 2.70 (m, 1H), 2.68 (dd, *J* = 8.5, 6.8 Hz, 2H), 1.91 – 1.85 (m, 2H); **¹³C NMR (101**

MHz, CDCl₃) δ 172.0, 141.9, 137.3, 129.1, 128.4(3), 128.3(8), 128.3, 126.6, 125.8, 72.6, 71.4, 70.2, 55.7(9), 55.7(5), 51.5, 36.7, 32.3, 31.2, 30.5; **HRMS (ESI)** *calcd.* for (C₂₃H₃₀NO₃) [M+H]⁺ : 368.2220, *found* 368.2221.



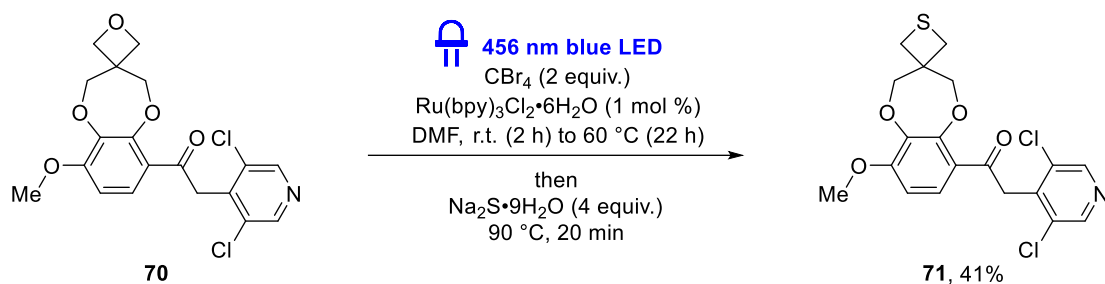
1-(1-(2,6-dimethylphenoxy)propan-2-yl)-3-((3-phenylpropoxy)methyl)azetidine

(83): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, mexiletine (0.8 mmol, 4.0 equiv.) and Na₂CO₃ (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1, with 5% Et₃N) to afford **83** (38.2 mg, 52% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.25 – 7.07 (m, 5H), 6.91 (d, *J* = 7.4 Hz, 2H), 6.82 (dd, *J* = 8.2, 6.6 Hz, 1H), 3.52 (d, *J* = 4.8 Hz, 1H), 3.49 – 3.39 (m, 5H), 3.35 (t, *J* = 6.4 Hz, 2H), 3.13 – 2.83 (m, 2H), 2.68 (p, *J* = 7.0 Hz, 1H), 2.64 – 2.51 (m, 3H), 2.19 (s, 6H), 1.89 – 1.75 (m, 2H), 1.05 (d, *J* = 6.4 Hz, 3H); **¹³C NMR (101 MHz, CDCl₃)** δ 155.7, 141.9, 130.8, 128.8, 128.4, 128.3, 125.7, 123.7, 74.0, 73.1, 70.1, 62.7, 56.8, 56.4, 32.2, 31.2, 30.4, 16.2, 14.7; **HRMS (ESI)** *calcd.* for (C₂₄H₃₄NO₂) [M+H]⁺ : 368.2584, *found* 368.2583.



ethyl **(3*R*,4*R*,5*S*)-4-acetamido-3-(pentan-3-yloxy)-5-((3-phenylpropoxy)methyl)azetidin-1-yl)cyclohex-1-ene-1-carboxylate (84):** In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with ether substrate (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in MeCN (2 mL). Then, oseltamivir (0.8 mmol, 4.0 equiv.) and Na₂CO₃ (2.0 mmol, 10.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 80 °C for 15 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1, with 5% Et₃N) to afford **84** (21.0 mg, 21% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.31 – 7.26 (m, 2H), 7.21 – 7.16 (m, 3H), 6.98 – 6.86 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.70 – 3.66 (m, 1H), 3.51 – 3.35 (m, 7H), 3.01 (d, *J* = 29.1 Hz, 2H), 2.73 – 2.66 (m, 3H), 2.62 – 2.51 (m, 2H), 2.31 (d, *J* = 18.2 Hz, 1H), 1.92 – 1.86 (m, 5H), 1.60 – 1.48 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 4H), 0.92 (q, *J* = 7.6 Hz, 6H); **¹³C NMR (101 MHz, CDCl₃)** δ 169.3, 166.9, 141.9, 133.3, 130.0, 128.4, 128.3, 125.8, 81.7, 72.6, 70.2, 68.6, 66.7, 60.8, 56.3, 55.9, 42.5, 32.3, 31.2, 30.1, 26.5, 26.2, 26.0, 23.5, 14.2, 9.8, 9.3; **HRMS (ESI)** *calcd.* for (C₂₉H₄₅N₂O₅) [M+H]⁺ : 501.3323, *found* 501.3322.

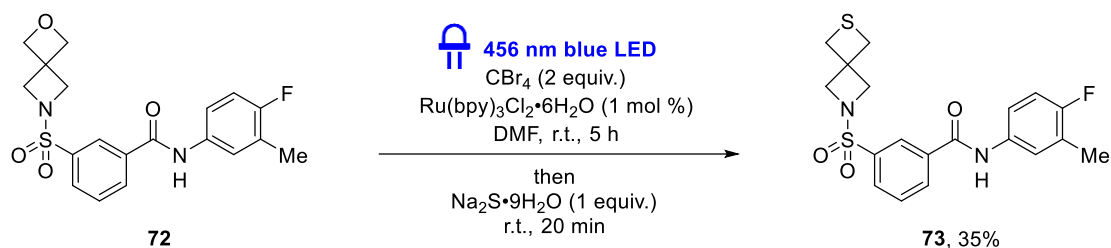
Late-stage editing of complex bioactive oxetanes



2-(3,5-dichloropyridin-4-yl)-1-(6-methoxy-2H,4H-spiro[benzo[*b*][1,4]dioxepine-3,3'-oxetan]-9-yl)ethan-1-one (70): It is a known compound from a previously reported synthesis with available analytical data ⁵: **¹H NMR (600 MHz, CDCl₃)** δ 8.50 (s, 2H), 7.55 (d, *J* = 8.8 Hz, 1H), 6.69 (d, *J* = 8.9 Hz, 1H), 4.71 – 4.53 (m, 8H), 4.52 (s, 2H), 3.92 (s, 3H); **¹³C NMR (151 MHz, CDCl₃)** δ 192.4, 156.0, 152.0, 147.2, 141.5, 140.3, 133.4, 125.4, 123.1, 106.5, 76.5, 76.3, 56.4, 45.4, 44.8; **HRMS (ESI) *calcd.*** for (C₁₉H₁₈Cl₂NO₅) [M+H]⁺ : 410.0557, *found* 410.0556.

2-(3,5-dichloropyridin-4-yl)-1-(6-methoxy-2H,4H-spiro[benzo[*b*][1,4]dioxepine-3,3'-thietan]-9-yl)ethan-1-one (71): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate **70** (0.1 mmol, 1.0 equiv.), CBr₄ (0.2 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 22 h. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 5:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (1 mL) and Na₂S·9H₂O (0.4 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at 90 °C for 20 min. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1) to afford **71** (17.4 mg, 41% yield) as yellow oil. It is a known compound with available analytical data ⁵: **¹H NMR (600 MHz, CDCl₃)** δ 8.52 (s, 2H), 7.57 (d, *J* = 8.8 Hz, 1H), 6.71 (d, *J* = 8.9 Hz, 1H), 4.64 (s, 2H), 4.46 (s, 2H), 4.33 (s, 2H), 3.93 (s, 3H), 3.19 (d, *J* = 10.0

Hz, 2H), 3.12 (d, $J = 10.0$ Hz, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ 192.3, 156.2, 152.5, 146.9, 142.1, 140.8, 133.6, 125.5, 123.2, 106.7, 78.2, 77.8, 56.4, 48.2, 45.4, 29.7; HRMS (ESI) *calcd.* for $(\text{C}_{19}\text{H}_{18}\text{Cl}_2\text{NO}_4\text{S}) [\text{M}+\text{H}]^+$: 426.0328, *found* 426.0334.



3-((2-oxa-6-azaspiro[3.3]heptan-6-yl)sulfonyl)-N-(4-fluoro-3-

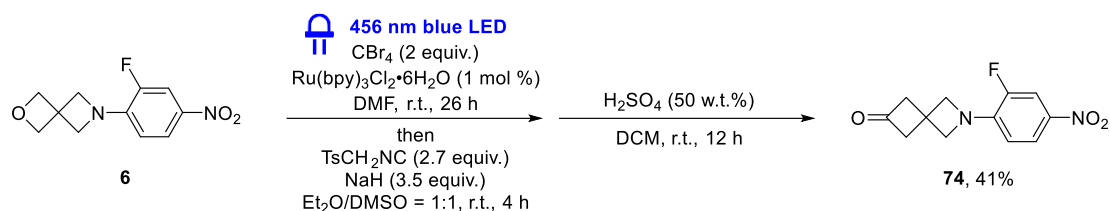
methylphenyl)benzamide (72): It is a known compound from a previously reported synthesis with available analytical data⁶: ^1H NMR (600 MHz, CDCl_3) δ 8.53 (s, 1H), 8.22 (s, 1H), 8.15 (d, $J = 7.6$ Hz, 1H), 7.89 (d, $J = 7.7$ Hz, 1H), 7.65 (t, $J = 7.8$ Hz, 1H), 7.50 (d, $J = 5.0$ Hz, 1H), 7.44 – 7.30 (m, 1H), 6.96 (t, $J = 8.9$ Hz, 1H), 4.55 (s, 4H), 3.88 (s, 4H), 2.25 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ 164.1, 158.3 (d, $J = 243.5$ Hz), 136.2, 135.1, 133.1 (d, $J = 2.9$ Hz), 132.8, 130.8, 129.8, 126.2, 125.4 (d, $J = 18.4$ Hz), 124.0 (d, $J = 4.6$ Hz), 119.8 (d, $J = 7.9$ Hz), 115.2 (d, $J = 23.5$ Hz), 80.0, 59.7, 37.5, 14.6 (d, $J = 3.2$ Hz); ^{19}F NMR (565 MHz, CDCl_3) δ -120.91; HRMS (ESI) *calcd.* for $(\text{C}_{19}\text{H}_{20}\text{FN}_2\text{O}_4\text{S}) [\text{M}+\text{H}]^+$: 391.1122, *found* 391.1124.

3-((2-thia-6-azaspiro[3.3]heptan-6-yl)sulfonyl)-N-(4-fluoro-3-

methylphenyl)benzamide (73): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate **72** (0.1 mmol, 1.0 equiv.), CBr_4 (0.2 mmol, 2.0 equiv.) and $\text{Ru(bpy)}_3\text{Cl}_2\cdot 6\text{H}_2\text{O}$ (0.001 mmol, 1 mol %) in anhydrous DMF (1 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at room temperature for 3 h. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 2:1). After removing the solvent by evaporation, the residue was re-

dissolved in DMF (1 mL) and $\text{Na}_2\text{S}\cdot 9\text{H}_2\text{O}$ (0.1 mmol, 1.0 equiv) was added in one portion. Then, the mixture was allowed to stir at room temperature for 20 min. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 1:1) to afford **73** (14.2 mg, 35% yield) as yellow oil. **^1H NMR (600 MHz, CDCl_3)** δ 8.29 – 8.12 (m, 3H), 7.94 (dt, $J = 7.8, 1.3$ Hz, 1H), 7.69 (t, $J = 7.8$ Hz, 1H), 7.52 (d, $J = 4.5$ Hz, 1H), 7.46 – 7.36 (m, 1H), 7.00 (t, $J = 8.9$ Hz, 1H), 3.79 (s, 4H), 3.14 (s, 4H), 2.28 (d, $J = 1.8$ Hz, 3H); **^{13}C NMR (126 MHz, CDCl_3)** δ 163.9, 158.4 (d, $J = 243.3$ Hz), 136.2, 135.4, 133.0 (d, $J = 3.1$ Hz), 132.6, 130.9, 129.9, 126.1, 125.6 (d, $J = 18.4$ Hz), 123.9, 119.7 (d, $J = 7.5$ Hz), 115.3 (d, $J = 23.6$ Hz), 63.5, 41.8, 36.2, 14.7 (d, $J = 3.3$ Hz); **^{19}F NMR (377 MHz, CDCl_3)** δ -120.92; **HRMS (ESI)** *calcd.* for $(\text{C}_{19}\text{H}_{20}\text{FN}_2\text{O}_3\text{S}_2)$ $[\text{M}+\text{H}]^+$: 407.0894, *found* 407.0892.

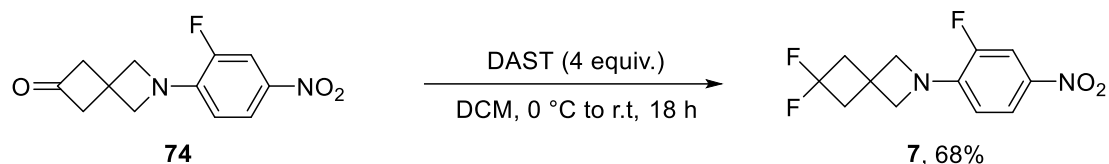
O-to-C transmutation to afford 1,1-difluorocyclobutane isostere



6 is a known compound with available analytical data⁷.

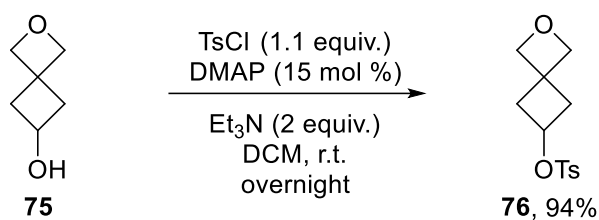
2-(2-fluoro-4-nitrophenyl)-2-azaspiro[3.3]heptan-6-one (74): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate **6** (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at room temperature for 24 hours. When cooling to room temperature, the residue was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 5:1). After removing the solvent by evaporation, the crude dibromide intermediate was obtained. Another 4 mL vial equipped with a magnetic stir bar was charged with the dibromide intermediate in anhydrous Et₂O (0.5 mL). Then, NaH (60 % dispersion in mineral oil, 0.7 mmol, 3.5 equiv.) was added to the mixture and followed by the addition of TsCH₂NC (0.54 mmol, 2.7 equiv.) in anhydrous DMSO (0.5 mL) at room temperature. The mixture was allowed to stir at room temperature for 4 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, DCM) to afford cyclobutane intermediate as yellow solid. Next, a 20 mL vial equipped with a magnetic stir bar was charged with cyclobutane intermediate in DCM (4 mL). Then, H₂SO₄ (50 w.t.%, 0.4 mL) was added and the mixture was allowed to stir at room temperature for 12 h. After completion of the reaction, the crude mixture was slowly quenched by saturated NaHCO₃ (aq.) and purified by silica gel chromatography (silica gel, DCM) to afford **74** (20.5 mg, 41% yield) as yellow solid (m.p.: 191-193 °C). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (dd, J = 8.9, 2.5 Hz, 1H), 7.85 (dd, J = 12.5, 2.4 Hz, 1H), 6.38 (t, J = 8.9

Hz, 1H), 4.39 (d, $J = 2.3$ Hz, 4H), 3.40 (s, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 204.1, 149.8 (d, $J = 244.4$ Hz), 143.5 (d, $J = 11.1$ Hz), 137.9 (d, $J = 7.4$ Hz), 121.6 (d, $J = 2.3$ Hz), 112.3 (d, $J = 23.2$ Hz), 111.7 (d, $J = 5.2$ Hz), 64.3 (d, $J = 1.9$ Hz), 57.8, 29.8 (d, $J = 3.1$ Hz); ^{19}F NMR (377 MHz, CDCl_3) δ -133.48; HRMS (ESI) *calcd.* for $(\text{C}_{12}\text{H}_{12}\text{FN}_2\text{O}_3)$ $[\text{M}+\text{H}]^+$: 251.0826, *found* 251.0827.



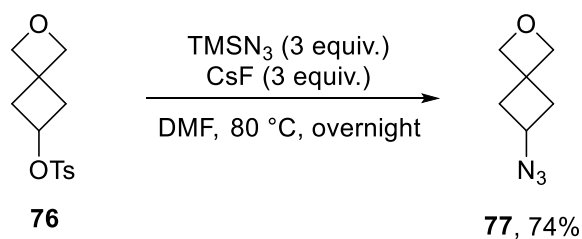
6,6-difluoro-2-(2-fluoro-4-nitrophenyl)-2-azaspiro[3.3]heptane (7): To a solution of **74** (0.1 mmol, 1.0 equiv.) with DCM (1 mL) in a 4 mL vial, DAST (0.4 mmol, 4 equiv.) was added in one portion at 0 °C. The mixture was then allowed to stir at room temperature for 18 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 5:1) to afford **7** (18.5 mg, 68% yield) as yellow solid (m.p.: 163-165 °C). ^1H NMR (400 MHz, CDCl_3) δ 7.97 – 7.89 (m, 1H), 7.84 (dd, $J = 12.5, 2.4$ Hz, 1H), 6.33 (t, $J = 8.9$ Hz, 1H), 4.25 (d, $J = 2.3$ Hz, 4H), 2.85 (t, $J = 11.9$ Hz, 4H); ^{13}C NMR (101 MHz, CDCl_3) δ 149.7 (d, $J = 244.4$ Hz), 143.5 (d, $J = 10.9$ Hz), 137.8 (d, $J = 7.7$ Hz), 121.6 (d, $J = 2.3$ Hz), 118.4 (t, $J = 279.8$), 112.2 (d, $J = 23.2$ Hz), 111.6 (d, $J = 5.1$ Hz), 64.1 (d, $J = 3.0$), 45.86 (t, $J = 23.3$ Hz), 29.02 (td, $J = 10.1, 2.8$ Hz); ^{19}F NMR (377 MHz, CDCl_3) δ -92.64, -133.61; HRMS (ESI) *calcd.* for $(\text{C}_{12}\text{H}_{12}\text{F}_3\text{N}_2\text{O}_2)$ $[\text{M}+\text{H}]^+$: 273.0845, *found* 273.0847.

Synthesis of the key precursor of respiratory syncytial virus inhibitor



75 is commercially available (BLD pharm).

2-oxaspiro[3.3]heptan-6-yl 4-methylbenzenesulfonate (76): To a solution of commercially available oxetane **75** (3.0 mmol, 1.0 equiv.), DMAP (0.45 mmol, 15 mol %) and Et₃N (6.0 mmol, 2.0 equiv.) in DCM (10 mL), TsCl (3.3 mmol, 1.1 equiv.) was added at room temperature. The reaction was allowed to stir overnight. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1) to afford **76** (752.4 mg, 94% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.87 – 4.28 (m, 5H), 2.63 – 2.53 (m, 2H), 2.45 (s, 3H), 2.36 – 2.27 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 144.9, 133.7, 129.9, 127.8, 83.0, 81.9, 69.6, 40.6, 36.2, 21.7; HRMS (ESI) *calcd.* for (C₁₃H₁₆NaO₄S) [M+Na]⁺ : 291.0662, *found* 291.0659.

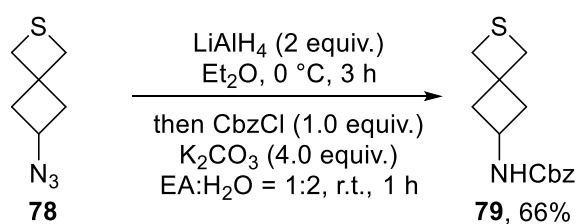


6-azido-2-oxaspiro[3.3]heptane (77): Under a nitrogen atmosphere, a solution of TMSN₃ (9.0 mmol, 3.0 equiv.) and CsF (9.0 mmol, 3.0 equiv., dried at 120 °C in oven for 3 hours) in DMF (3 mL) was pre-stirred for 20 min. Then, a solution of oxetane **76** in DMF (3 mL) was added at room temperature. The reaction was allowed to stir overnight at 80 °C. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **77** (310.6 mg, 74% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 4.68 (s, 2H), 4.63 (s, 2H), 3.72 (p, *J* = 7.5 Hz, 1H), 2.65 – 2.56 (m, 2H), 2.28 – 2.19 (m, 2H); ¹³C NMR (101

MHz, CDCl₃) δ 83.3, 82.3, 50.2, 39.1, 37.2; **HRMS (ESI)** *calcd.* for (C₆H₁₀N₃O) [M+H]⁺ : 140.0818, *found* 140.0819.

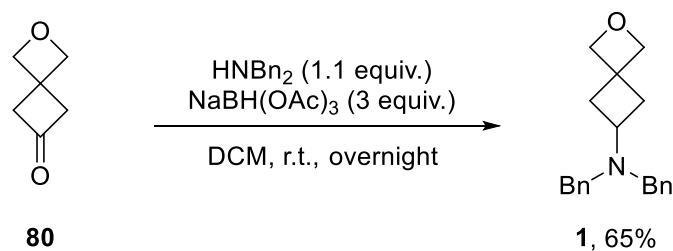


6-azido-2-thiaspiro[3.3]heptane (78): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate **77** (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 h. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (2 mL) and Na₂S·9H₂O (0.8 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at room temperature for 30 min. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 50:1) to afford **78** (20.8 mg, 67% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 3.74 (p, *J* = 7.6 Hz, 1H), 3.23 (s, 2H), 3.20 (s, 2H), 2.65 – 2.55 (m, 2H), 2.14 – 2.04 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 49.9, 43.0, 41.9, 38.6, 38.1; **HRMS (ESI)** *calcd.* for (C₆H₁₀N₃S) [M+H]⁺ : 156.0590, *found* 156.0592.



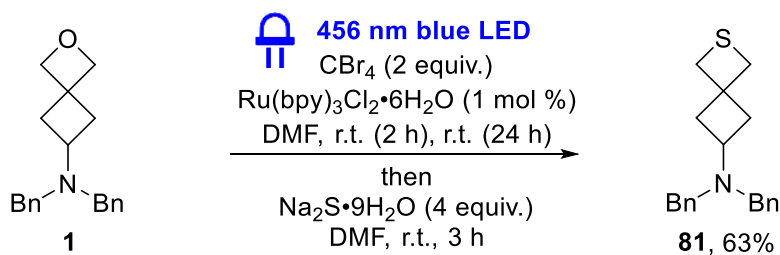
benzyl (2-thiaspiro[3.3]heptan-6-yl)carbamate (79): To a solution of oxetane **78** (0.1 mmol, 1.0 equiv.) in anhydrous Et₂O, LiAlH₄ (0.2 mmol, 2.0 equiv.) was added dropwise at 0 °C. The mixture was allowed to stir at 0 °C for 3 hours. After quenching this reaction with one drop of H₂O, the mixture was filtered and the solvent was removed by evaporation. The residue was re-dissolved in ethyl acetate (0.5 mL)/H₂O (1 mL) with addition of K₂CO₃ (0.4 mmol, 4.0 equiv.) and CbzCl (0.1 mmol, 1.0 equiv.). Then, the mixture was allowed to stir at room temperature for 1 hour. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 2:1) to afford **79** (17.4 mg, 66% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.33 (q, *J* = 7.9, 6.5 Hz, 5H), 5.07 (s, 2H), 4.82 (s, 1H), 4.01 (d, *J* = 7.7 Hz, 1H), 3.25 (s, 2H), 3.15 (s, 2H), 2.77 – 2.55 (m, 2H), 1.96 – 1.80 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 155.3, 136.3, 128.5, 128.2, 66.7, 44.9, 41.8, 40.8, 38.8, 37.9; **HRMS (ESI)** *calcd.* for (C₁₄H₁₈NO₂S) [M+H]⁺ : 264.1053, *found* 264.1056.

Synthesis of the key precursor of cyclin-dependent kinase 2 inhibitor



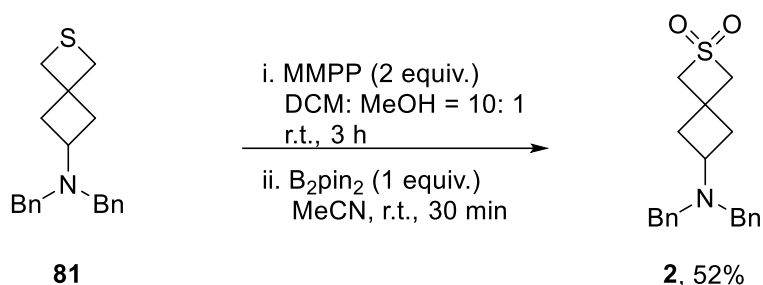
80 is commercially available (BLD pharm).

***N,N*-dibenzyl-2-oxaspiro[3.3]heptan-6-amine (1):** To a solution of the 2-oxaspiro[3.3]heptan-6-one **80** (0.2 mmol, 1.0 equiv.) and HNBn₂ (0.22 mmol, 1.1 equiv.) in DCM (0.5 mL), NaBH(OAc)₃ (0.6 mmol, 3.0 equiv.) was added in portions. The mixture was allowed to stir overnight at room temperature. After quenching this reaction with saturated solution of NaHCO₃, the mixture extracted with DCM for three times and the combined organic phase was dried over with anhydrous Na₂SO₄. After concentration of the organic phases in vacuo, the resulting crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 20:1) to afford **1** (38.2 mg, 65% yield) as yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.58 – 7.07 (m, 10H), 4.70 (s, 2H), 4.60 (s, 2H), 3.50 (s, 4H), 3.05 – 2.90 (m, 1H), 2.42 – 2.26 (m, 2H), 2.13 – 1.99 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 138.7, 129.1, 128.1, 126.9, 84.7, 82.5, 54.5, 52.8, 38.6, 36.6; HRMS (ESI) *calcd.* for (C₂₀H₂₄NO) [M+H]⁺ : 294.1852, *found* 294.1855.



***N,N*-dibenzyl-2-thiaspiro[3.3]heptan-6-amine (81):** In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane substrate **1** (0.05 mmol, 1.0 equiv.), CBr₄ (0.1 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O

(0.0005 mmol, 1 mol %) in anhydrous DMF (0.5 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at r.t. for 24 h. When cooling to room temperature, the mixture was filtered by 10 mL silica gel and washed with 30 mL solvent (hexanes:EtOAc = 10:1). After removing the solvent by evaporation, the residue was re-dissolved in DMF (0.25 mL) and Na₂S·9H₂O (0.2 mmol, 4.0 equiv) was added in one portion. Then, the mixture was allowed to stir at room temperature for 3 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 20:1) to afford **81** (9.7 mg, 63% yield) as yellow oil. ¹H NMR (600 MHz, CDCl₃) δ 7.33 – 7.25 (m, 10H), 3.46 (s, 4H), 3.22 (s, 2H), 3.14 (s, 2H), 3.02 – 2.94 (m, 1H), 2.38 – 2.28 (m, 2H), 1.88 – 1.82 (m, 2H); ¹³C NMR (151 MHz, CDCl₃) δ 138.9, 129.1, 128.1, 126.9, 54.6, 52.5, 42.8, 41.6, 39.8, 38.2; HRMS (ESI) *calcd.* for (C₂₀H₂₄NS) [M+H]⁺ : 310.1624, *found* 310.1627.

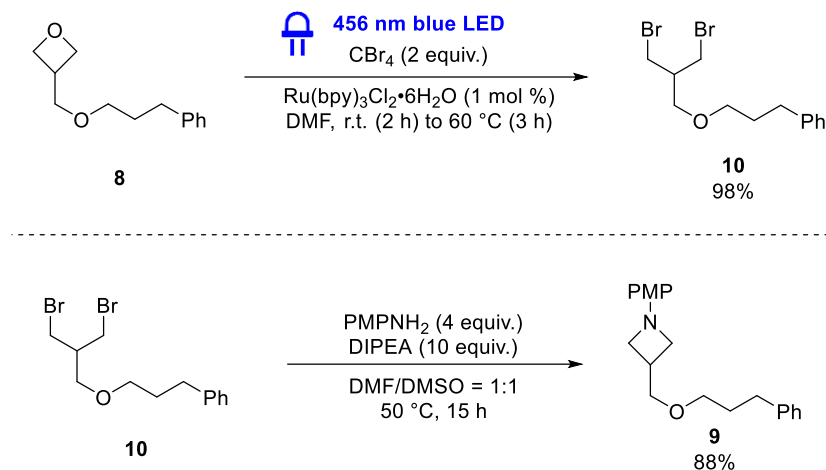


6-(dibenzylamino)-2-thiaspiro[3.3]heptane 2,2-dioxide (2): To a solution of the *N,N*-dibenzyl-2-thiaspiro[3.3]heptan-6-amine (0.05 mmol, 1 equiv.) in DCM: MeOH =10: 1 (0.5 mL: 0.05 mL), magnesium monoperoxyphthalate hexahydrate (MMPP, 0.1 mmol, 2 equiv.) was added in portions. The mixture was allowed to stir for 3 hours at room temperature. After completion of the reaction, the mixture was concentrated in vacuo. The resulting crude mixture was purified by silica gel chromatography (silica gel, DCM:MeOH = 10:1) to afford the pure intermediate. To the mixture of this intermediate and B₂pin₂ (0.05 mmol, 1 equiv.) in a flask under nitrogen, acetonitrile (0.25 mL) was added and the mixture was allowed to stir at room temperature for 30

min. After completion of the reaction, the mixture was concentrated in vacuo. The resulting crude mixture was purified by silica gel chromatography (silica gel, DCM:MeOH = 10:1) to afford **2** (8.8 mg, 52% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.63 – 7.01 (m, 10H), 4.10 (s, 2H), 4.06 (s, 2H), 3.50 (s, 4H), 3.24 – 3.06 (m, 1H), 2.43 – 2.30 (m, 2H), 2.26 – 2.13 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 138.4, 129.0, 128.2, 127.1, 75.6, 75.2, 55.0, 53.7, 40.6, 22.7; **HRMS (ESI)** *calcd.* for (C₂₀H₂₄NO₂S) [M+H]⁺ : 342.1522, *found* 342.1527.

5. Mechanistic Investigations

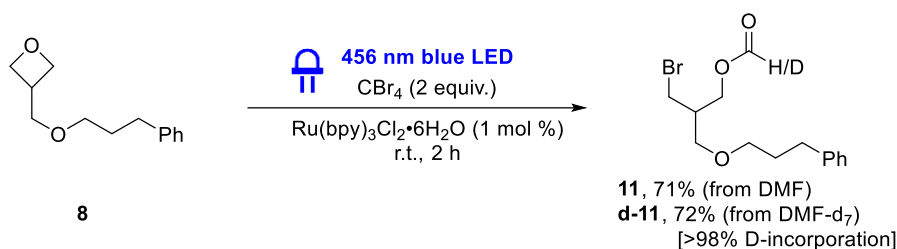
Control experiments to probe dibromide intermediate



Supplementary Figure 1. Inspection of the dibromide intermediate.

(3-(3-bromo-2-(bromomethyl)propoxy)propyl)benzene (10): In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane **8** (0.2 mmol, 1.0 equiv.), CBr_4 (0.4 mmol, 2.0 equiv.) and $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. Then, the blue LED was turned off and the mixture was allowed to stir at 60 °C for 3 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 30:1) to afford **10** (68.6 mg, 98% yield) as yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.35 – 7.27 (m, 2H), 7.25 – 7.10 (m, 3H), 3.64 – 3.51 (m, 4H), 3.52 – 3.42 (m, 4H), 2.70 (dd, J = 8.5, 6.8 Hz, 2H), 2.32 (p, J = 5.7 Hz, 1H), 1.95 – 1.84 (m, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 141.7, 128.4, 128.3, 125.8, 70.4, 70.0, 42.9, 33.2, 32.3, 31.1; HRMS (ESI) *calcd.* for $(\text{C}_{13}\text{H}_{19}\text{Br}_2\text{O})$ $[\text{M}+\text{H}]^+$: 348.9797, *found* 348.9794.

Control experiments to probe alkyl formate intermediate



Supplementary Figure 2. Inspection of the formate byproduct by interrupting the bromination.

3-bromo-2-((3-phenylpropoxy)methyl)propyl formate (11**):** In a glovebox under nitrogen atmosphere, a 4 mL vial equipped with a magnetic stir bar was charged with oxetane **8** (0.2 mmol, 1.0 equiv.), CBr₄ (0.4 mmol, 2.0 equiv.) and Ru(bpy)₃Cl₂·6H₂O (0.002 mmol, 1 mol %) in anhydrous DMF (2 mL). The reaction vial was sealed and taken out of the glovebox. The mixture was allowed to stir at room temperature under 20 W blue LED (456 nm) illumination for 2 hours. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **11** (44.7 mg, 71% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 8.08 (s, 1H), 7.40 – 7.26 (m, 2H), 7.25 – 7.09 (m, 3H), 4.34 – 4.21 (m, 2H), 3.59 – 3.39 (m, 6H), 2.77 – 2.63 (m, 2H), 2.42 – 2.30 (m, 1H), 1.97 – 1.84 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 160.7, 141.8, 128.4, 128.3, 125.8, 70.4, 68.8, 62.9, 40.5, 32.3, 31.8, 31.1; **HRMS (ESI) *calcd.* for (C₁₄H₁₉BrNaO₃) [M+Na]⁺ : 337.0410, *found* 337.0411.**

3-bromo-2-((3-phenylpropoxy)methyl)propyl formate-*d* (d-11**):** Based on the above procedure to prepare **11**, **d-11** was synthesized by employing DMF-d₇ as solvent. After completion of the reaction, the crude mixture was purified by silica gel chromatography (silica gel, hexanes:EtOAc = 10:1) to afford **d-11** (45.5 mg, 72% yield) as yellow oil. **¹H NMR (400 MHz, CDCl₃)** δ 7.35 – 7.26 (m, 2H), 7.26 – 7.11 (m, 3H), 4.36 – 4.20 (m, 2H), 3.65 – 3.32 (m, 6H), 2.74 – 2.63 (m, 2H), 2.42 – 2.29 (m, 1H), 1.96 – 1.82 (m, 2H); **¹³C NMR (101 MHz, CDCl₃)** δ 141.8, 128.5, 128.3, 125.8, 70.4, 68.8, 62.8, 40.4, 32.2, 31.8, 31.1.

6. Density Functional Theory (DFT) Calculations

Computational methods

Kohn-Sham density functional theory (KS-DFT) calculations were performed with *Gaussian 16* rev. B.01.⁸ The global hybrid DFT functional M06-2X⁹ with the def2-SVPD^{10,11} Karlsruhe-family basis set for Br atom and def2-SVP^{10,12} basis set for all other atoms (this mixed basis set is denoted BS1) with implicit SMD continuum solvation model¹³ for N,N-dimethyl formamide (DMF) solvent was used for geometry optimization. The “D” in def2-SVPD basis set denotes diffuse functions which are important for the correct description of anionic electron distributions.¹⁴⁻¹⁶ Minima and transition structures on the potential energy surface (PES) were confirmed as such by harmonic frequency analysis, showing respectively zero and one imaginary frequency. M06-2X was chosen as it has shown good accuracy in the study of organocatalytic systems.¹⁷⁻²⁷ For the SMD(DMF)-M06-2X/BS1 optimized structures, single point (SP) corrections were performed using M06-2X functional and def2-TZVPD^{10,11} basis set for Br atom and def2-TZVP^{10,12} basis set for all other atoms (denoted BS2) in the implicit SMD continuum for DMF solvent to improve upon the accuracy of the calculated energies. All DFT calculations were submitted using our automation toolkit CHEMSMART.²⁸

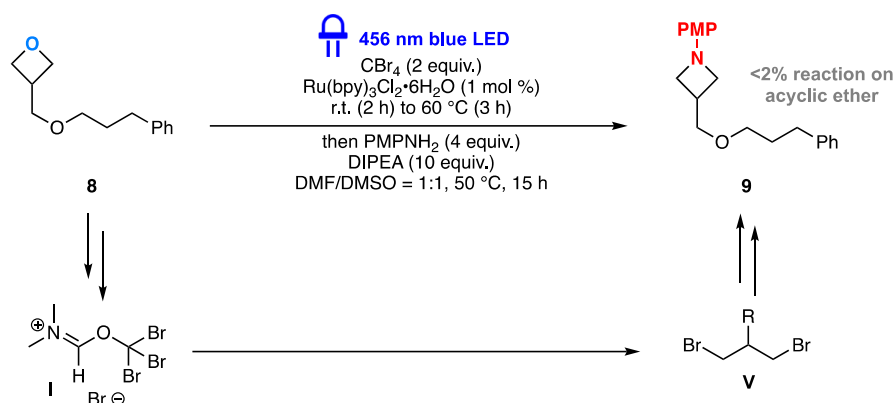
Gibbs energies were evaluated at the room temperature of 25°C, using Grimme’s scheme of quasi-RRHO treatment of vibrational entropies,²⁹ using the CHEMSMART code. Vibrational entropies of frequencies below 100 cm⁻¹ were obtained according to a free rotor description, using a smooth damping function to interpolate between the two limiting descriptions. The free energies reported in Gaussian from gas-phase optimisation were further corrected using standard concentration of 1 mol/L,³⁰⁻³² which were used in solvation calculations, instead of the gas-phase 1atm used by default in Gaussian program. Unless otherwise stated, the final SMD(DMF)-M06-2X/BS2//M06-2X/BS1 Gibbs energies are used for discussion throughout. *All Gibbs energy values in the text and figures are quoted in kcal/mol.*

Non-covalent interactions (NCIs) were analyzed using NCIPLOT³³ calculations. The *.wfn* files for NCIPLOT were generated at M06-2X/BS1 level of theory. NCI indices calculated with NCIPLOT were visualized at a gradient isosurface value of $s = 0.5$ au. These are colored according to the sign of the second eigenvalue (λ_2) of the Laplacian of the density ($\nabla^2\rho$) over the range of -0.1 (blue = attractive) to $+0.1$ (red = repulsive). Molecular orbitals are visualized using an isosurface value of 0.05 au throughout.

All molecular structures and molecular orbitals are visualized using *PyMOL*³⁴ software, which *.pse* files were prepared using our CHEMSMART package.

Model reaction

Supplementary Figure 3 shows the model reaction that we used for computational studies of the reaction mechanism for the conversion of species **I** to species **V**.



Supplementary Figure 3. Model reaction used in computational modelling.

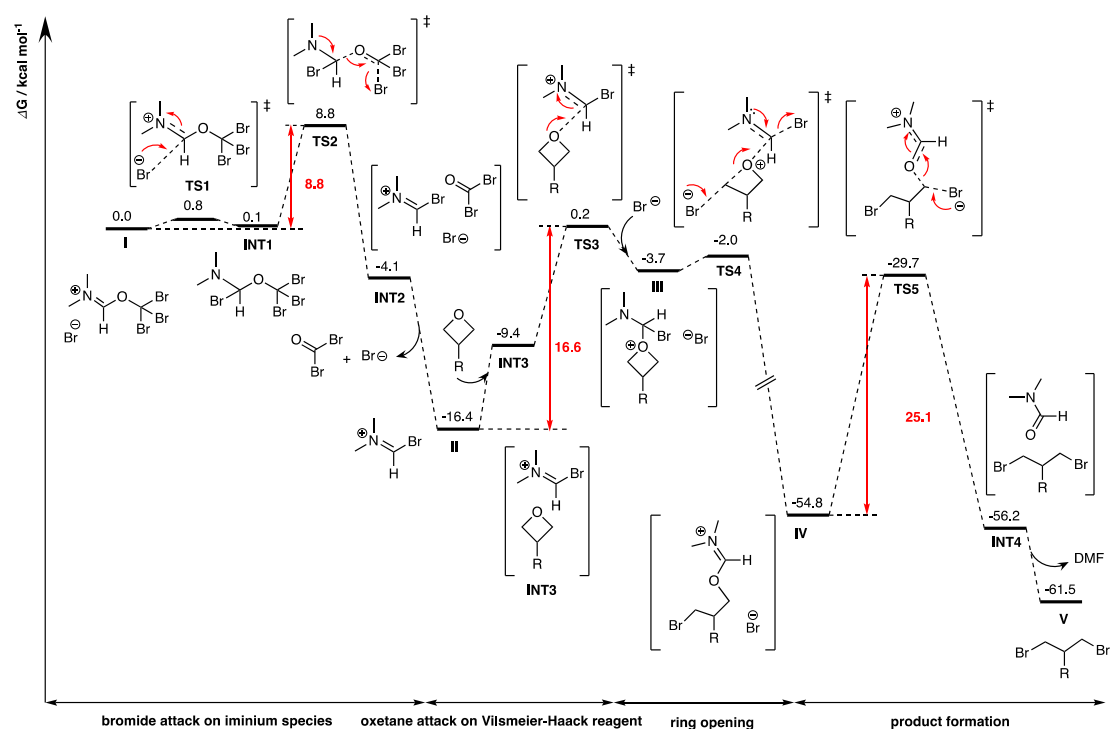
Conformational Considerations

Conformational sampling was performed for the cationic iminium species of complex **I** using Grimme's *CREST* program,^{35,36} which used metadynamics (MTD) with genetic z-matrix crossing (GC) performed at the GFN2-xTB³⁷⁻³⁹ extended semiempirical tight-binding level of theory with *opt=vtight* option. Two distinct conformers were located after further DFT optimization. The lowest energy structure is used for all subsequent studies.

Most favourable pathway

The most favourable reaction pathway occurs when the iminium species in complex **I** is attacked by bromide anion, via **TS1**, with a very small barrier of 0.8 kcal/mol, to give an almost isoenergetic species **INT1** (Supplementary Figure 4). This step is reversible, giving complex **I** and **INT1** in equilibrium. Next, **INT1** can undergo a C–O bond cleavage via **TS2**, with a barrier of 8.8 kcal/mol from **I**, to give the Vilsmeier-Haack reagent (**II**), carbonyl bromide (Br₂CO) and bromide anion as complex **INT2**. The release of Br₂CO and Br[−] gives **II** which is highly exergonic, being downhill of starting complex **I** by -16.4 kcal/mol. Thus, the formation of give Vilsmeier-Haack reagent **II** is highly thermodynamically favourable.

The subsequent addition of oxetane substrate gives complex **INT3** that is 7.0 kcal/mol uphill of **II**. The attack of the imine group by the oxetane oxygen atom occurs via **TS3**, with a barrier of 16.6 kcal/mol from the Vilsmeier-Haack reagent **II**. Next, bromide anion attacks the carbon atom on the oxetane ring, via **TS4**, with a small barrier of 1.7 kcal/mol from complex **III**, to give ring-opened species **IV**. This step is highly exergonic and thermodynamically favourable, as the ring-opened species **IV** lies 51.1 kcal/mol downhill of complex **III**. Thus, from the Vilsmeier-Haack reagent **II**, once the oxetane attacks the iminium to form complex **III**, the subsequent ring opening is facile and both kinetically and thermodynamically favourable, giving ring-opened intermediate **IV**. This step has an overall barrier of 16.6 kcal/mol (from **II** to **TS3**) and is thermodynamically downhill by 38.4 kcal/mol (from **II** to **IV**).



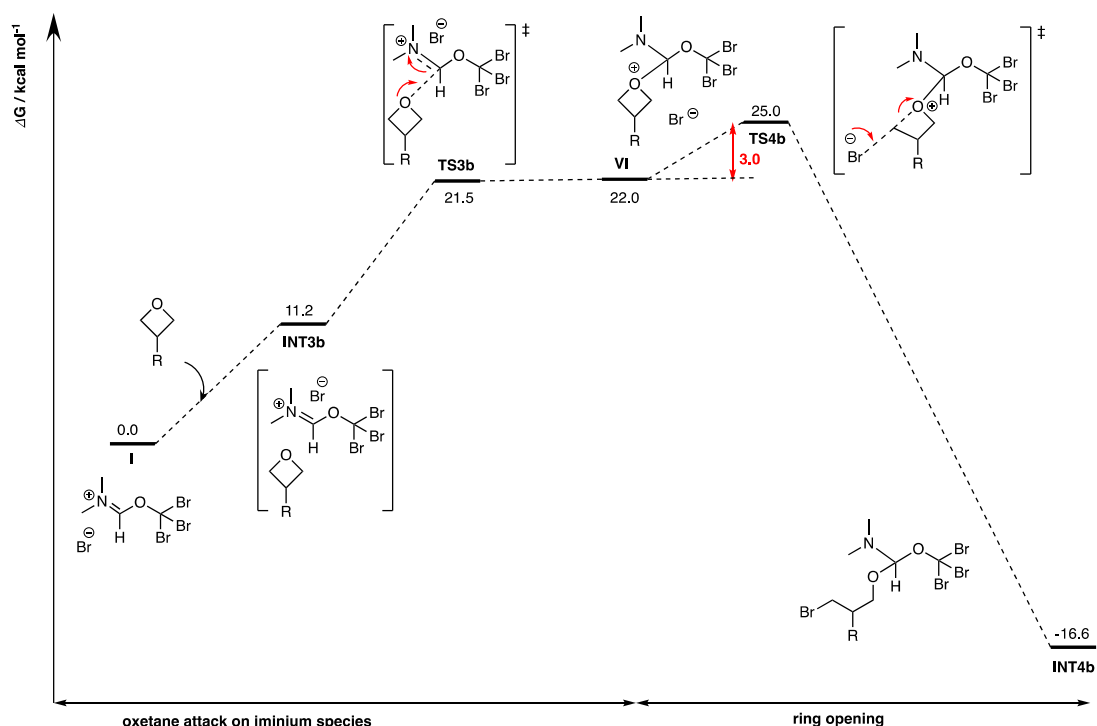
Supplementary Figure 4. Gibbs energy profile for the conversion of complex **I to complex **V**.**

Next, the bromide anion attacks the C–O bond through S_N2 mechanism via **TS5**, with an overall barrier of 25.1 kcal/mol from species **IV**, to give an almost isoenergetic but slightly downhill dibromide complexed with DMF molecule, **INT4**. The release of DMF molecule from this complex is exergonic and gives the dibromide, **V**, at -61.5 kcal/mol, which is 6.7 kcal/mol downhill of **IV**. Overall, the formation of **V** from **I** is thermodynamically favourable, with Gibbs energy of reaction, $\Delta G_r = -61.5$ kcal/mol. The rate-limiting step is the formation of second C–Br bond via **TS5**, with a barrier of 25.1 kcal/mol.

Oxetane reactivity with complex **I**

For complex **I**, we also considered the possibility that the oxetane oxygen directly attacks the imine group of the iminium species. The Gibbs energy profile is shown in Supplementary Figure 5. The formation of **I** with oxetane gives complex **INT3b**, which is uphill by 11.2 kcal/mol. Subsequently, the oxetane oxygen can attack the imine group, via **TS3b**, which has a barrier of 21.5 kcal/mol from species **I**, to give a rather unstable species **VI**. This species can undergo ring opening via **TS4b**, with a barrier of 3.0

kcal/mol from **VI** (overall barrier of 25.0 kcal/mol from complex **I**), to given complex **INT4b**, which is downhill of complex **I**, by -16.6 kcal/mol.



Supplementary Figure 5. Gibbs energy profile for the attack of complex **I to by oxetane.**

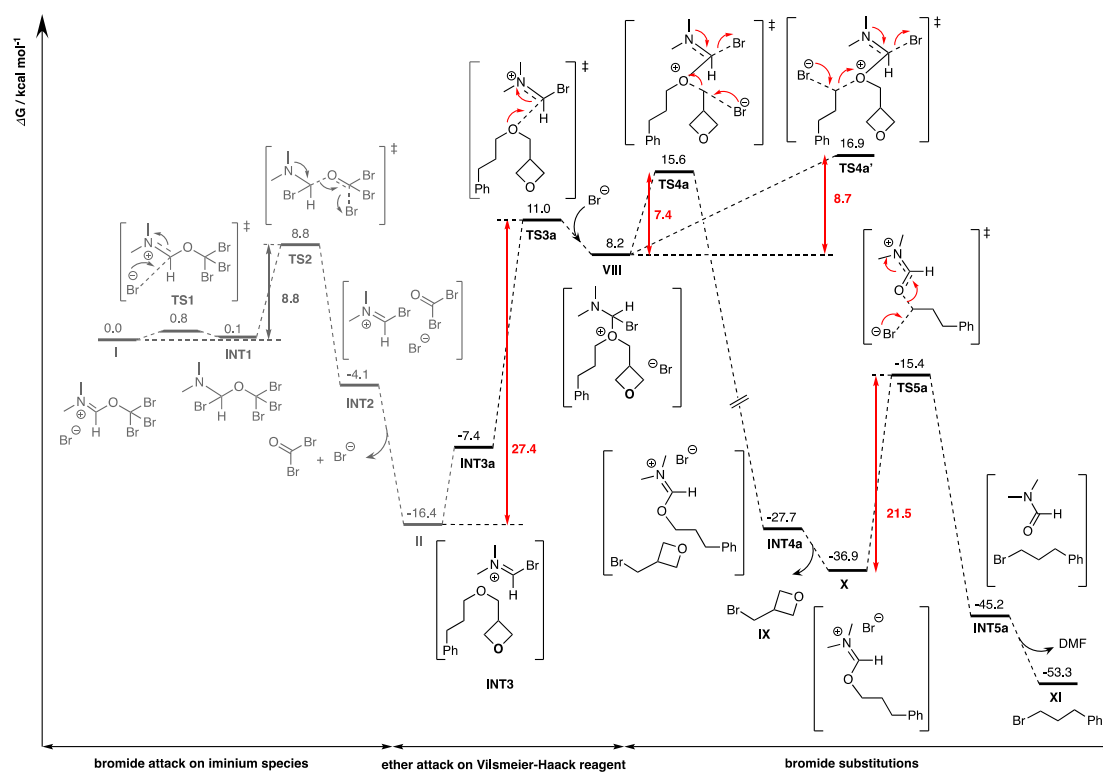
Although the formation of complex **INT4b** from **I** is thermodynamically favourable and kinetically feasible, however, complex **I** will be preferentially attacked by bromide ion, via **TS2** with a barrier of 8.8 kcal/mol (Supplementary Figure 4), instead of attacked by oxetane oxygen, via **TS3b**, with a higher barrier of 21.5 kcal/mol (Supplementary Figure 5). Thus, the formation of the Vilsmeier-Haack reagent **II** is kinetically favoured over the reaction of oxetane oxygen with complex **I**, by 12.7 kcal/mol (rate ratio of about 2 billion : 1 using simple transition state theory as an estimate at room temperature, Section **Simple transition state theory (TST) for rate estimation**).

Chemoselectivity between cyclic and acyclic ethers

After the full mechanism for the conversion of species **I** to species **V** is elucidated (Supplementary Figure 4), we focus on the steps for the oxygen attack on the iminium

group of the Vilsmeier-Haack reagent **II** (**TS3**) and the subsequent bromide attack (**TS4**) to understand the chemoselectivity outcomes (comparing attack by oxetane oxygen vs acyclic ether oxygen). After the formation of the Vilsmeier-Haack reagent **II**, it can form complex with substrate to give **INT3a** (conformer of **INT3**, Supplementary Figure 4) where the ether oxygen is close to the iminium carbon. This complex is 9.0 kcal/mol uphill of **II**. The subsequent attack of iminium group by ether oxygen occurs via **TS3a**, with a barrier of 27.4 kcal/mol from **II**, to give complex **VIII**, which is uphill of **INT3a** by 15.6 kcal/mol. The bromide anion can then attack **VIII** at two different carbon positions, via **TS4a** or **TS4a'**. From **VIII**, attack on the carbon adjacent to the oxetane group, via **TS4a**, gives a barrier of 7.4 kcal/mol, but attack on the other carbon, via **TS4a'**, gives a higher barrier of 8.7 kcal/mol.

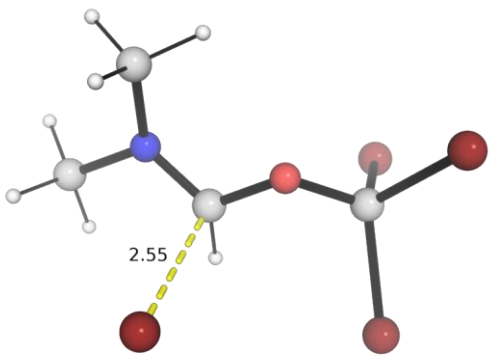
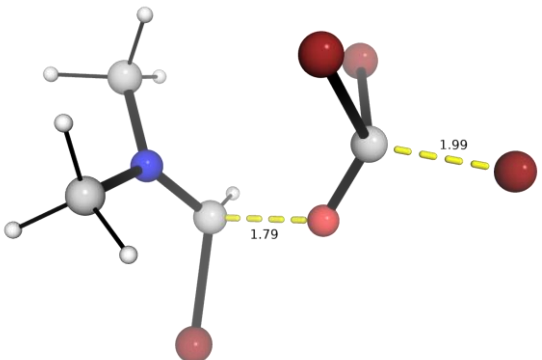
We observe that for the major pathway shown in Supplementary Figure 4, the attack on iminium carbon by oxetane oxygen (**TS3**) has a higher barrier than the subsequent ring opening by bromide anion (**TS4**). On the other hand, in Supplementary Figure 6 for the competing pathway, the attack on iminium carbon by ether oxygen (**TS3a**) has a lower barrier than the subsequent C–Br bond formation by bromide anion (**TS4a**). This is likely attributed to the fact that the release of ring strain makes the ring opening (**TS4**) for C–Br bond formation more facile than the C–Br bond formation in **TS4a** which does not benefit from release of ring strain.

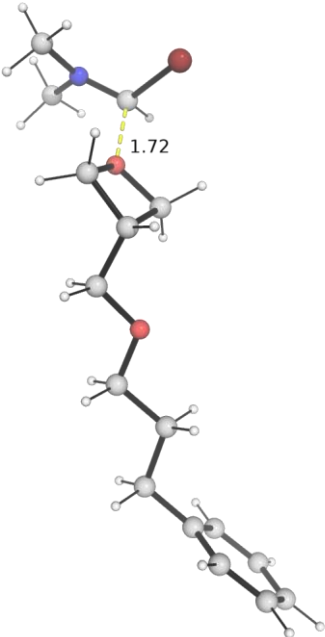
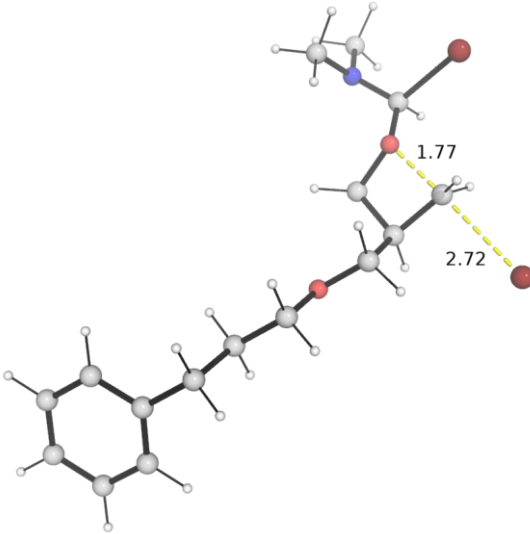
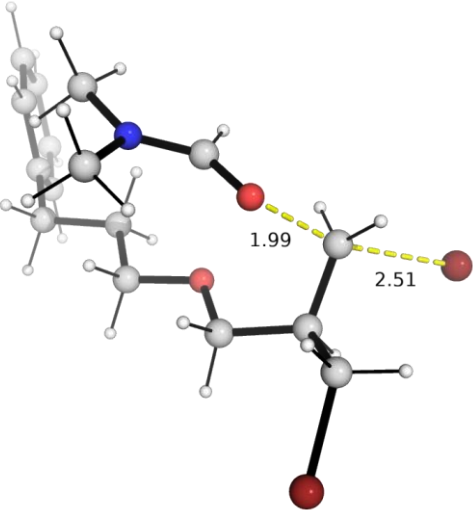
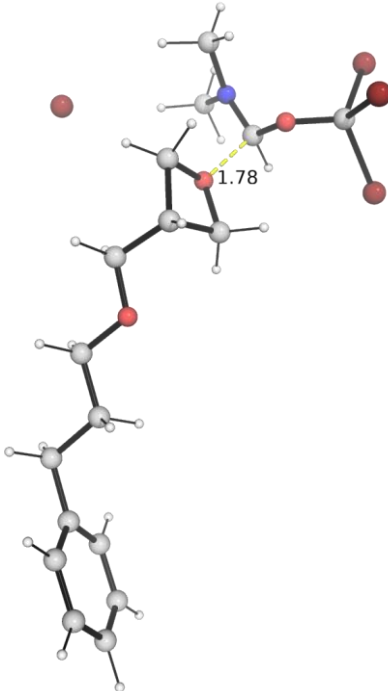


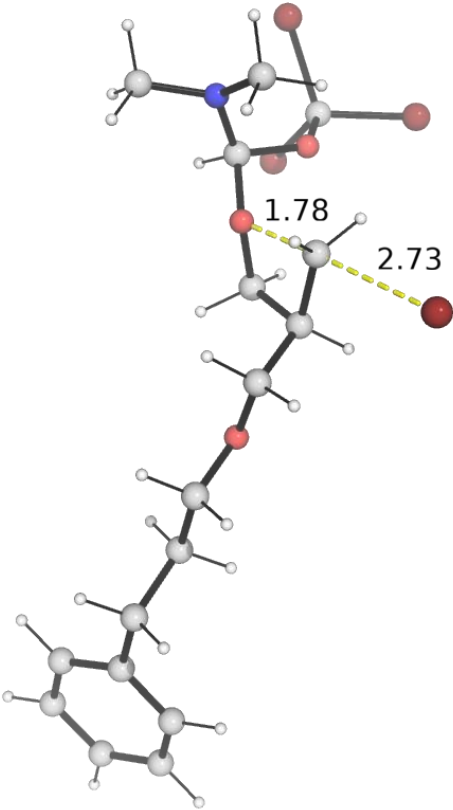
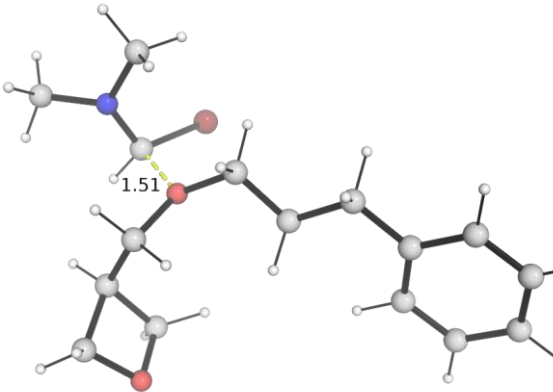
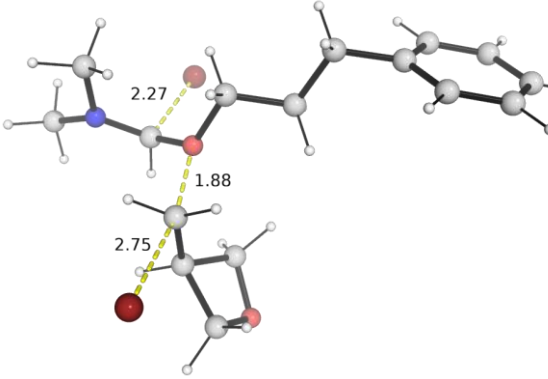
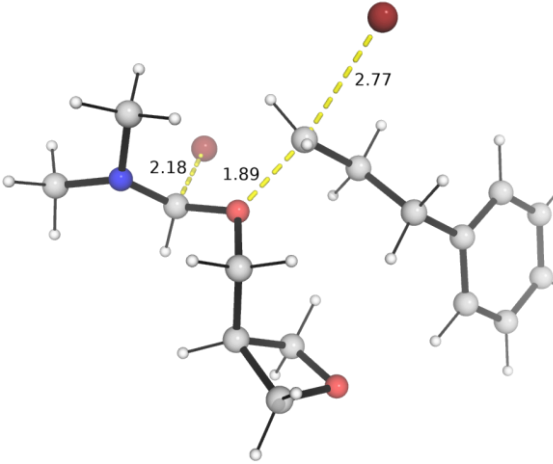
Supplementary Figure 6. Gibbs energy profile for chemoselectivity studies.

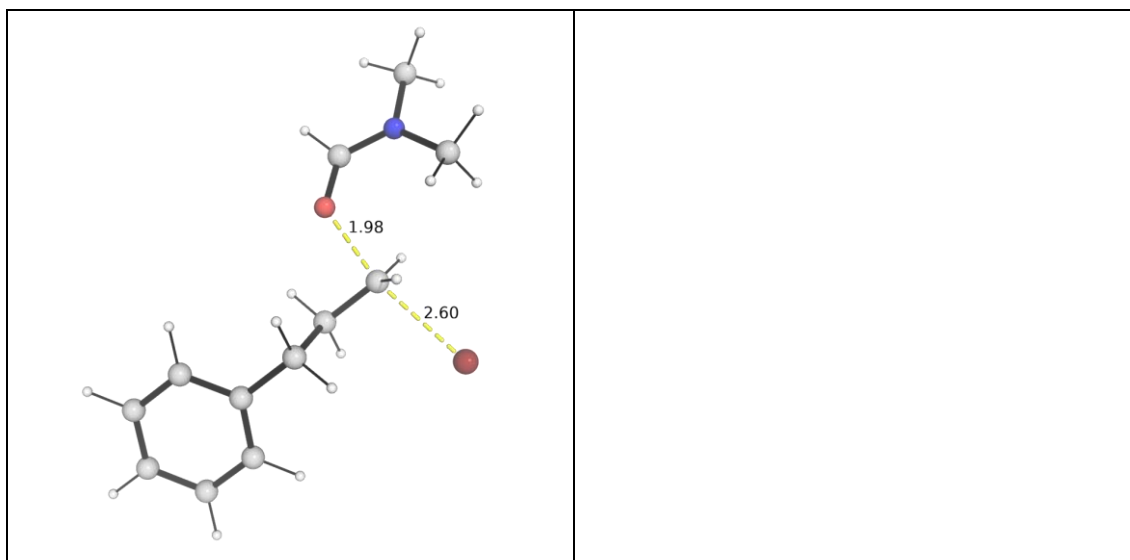
DFT-optimised structures

Selected DFT-optimised structures are shown in Supplementary Figure 7.

TS1	TS2
$\Delta G^\ddagger = 0.8$	$\Delta G^\ddagger = 8.8$
	
TS3	TS4
$\Delta G^\ddagger = 0.2$	$\Delta G^\ddagger = -2.0$

	
TS5	TS3b
$\Delta G^\ddagger = -29.7$	$\Delta G^\ddagger = 21.5$
	
TS4b	TS3a
$\Delta G^\ddagger = 25.0$	$\Delta G^\ddagger = 11.0$

	
TS4a	TS4a'
$\Delta G^\ddagger = 15.6$	$\Delta G^\ddagger = 16.9$
	
TS5a	
$\Delta G^\ddagger = -15.4$	



Supplementary Figure 7. DFT-optimized structures for the transition states.

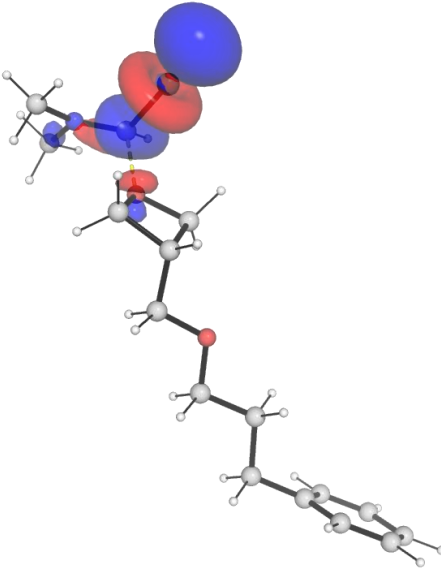
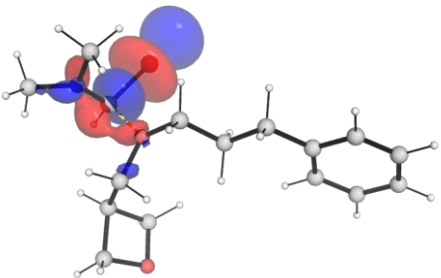
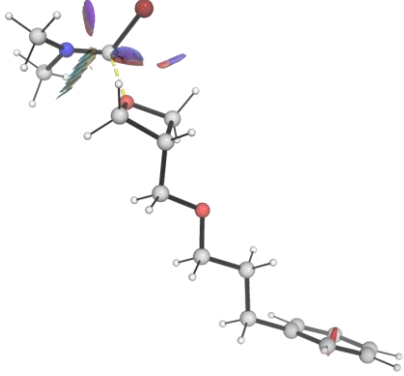
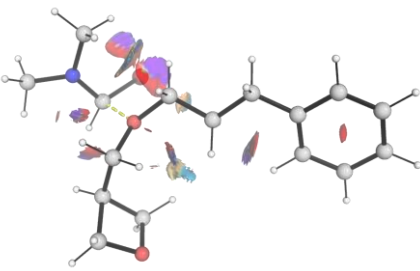
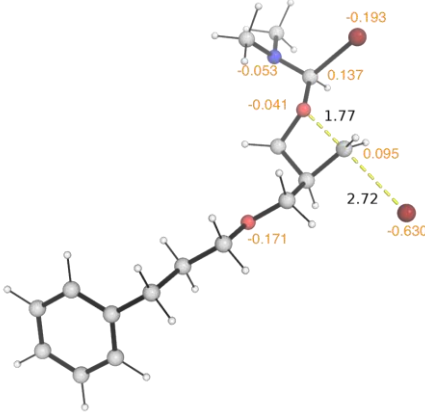
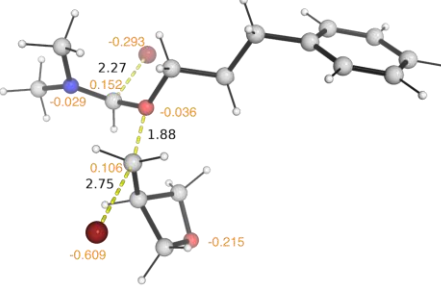
Molecular origins of chemoselectivity

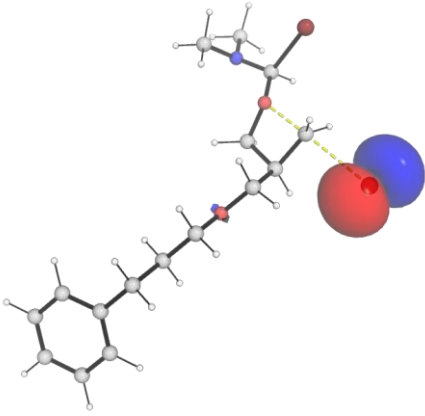
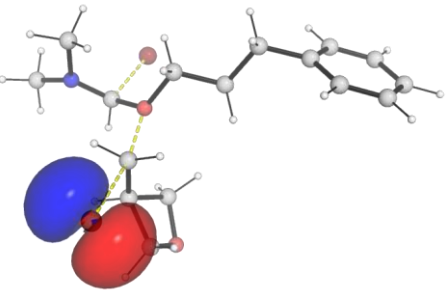
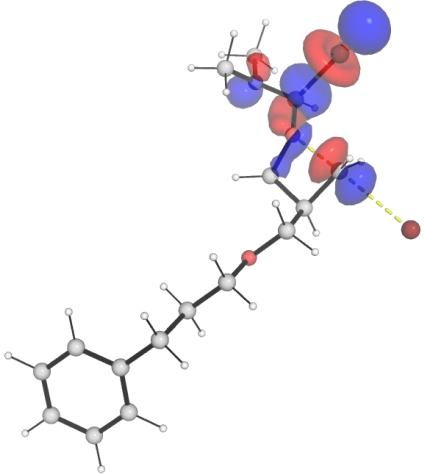
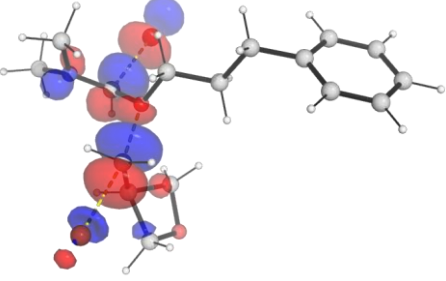
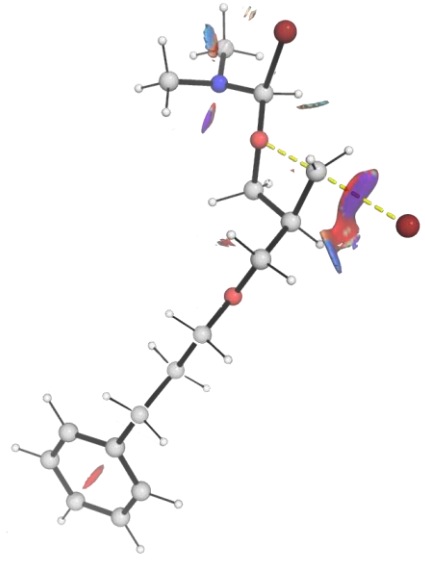
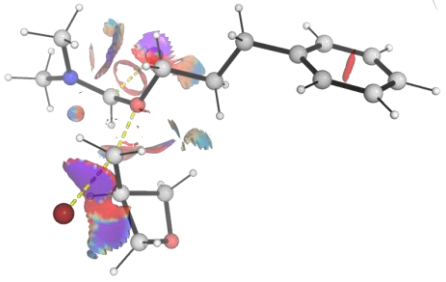
Comparing the barriers of **TS3** and **TS3a**, we see that **TS3** has a lower barrier by 10.8 kcal/mol than **TS3a**. This translates to a kinetic preference for **TS3** over **TS3a** by a factor of 30 million : 1, using simple transition state theory. In other words, attack on the iminium carbon of the Vilsmeier-Haack reagent **II** by the oxetane oxygen is much more favourable than that by the ether oxygen.

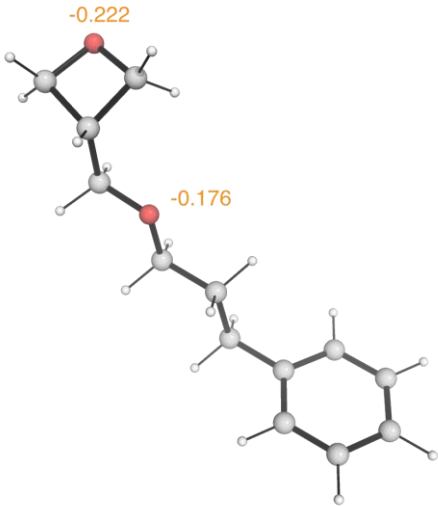
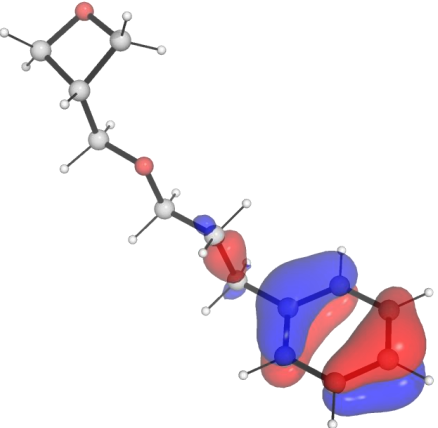
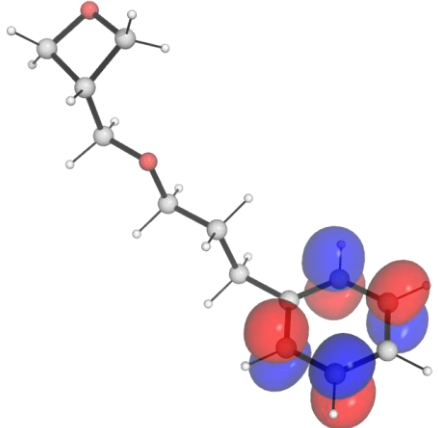
Analysis of Hirshfeld charges⁴⁰ (charge scheme less dependent on DFT basis sets) on substrate **8** indicates that the oxetane oxygen atom has a more negative charge at -0.222 a.u., which is more negative than the charge at ether oxygen, at -0.176 a.u., by 0.046 a.u., suggesting that the oxetane oxygen is more nucleophilic than the ether oxygen. The Fukui reactivity index (f^-) also shows that the oxetane oxygen is much more nucleophilic than the ether oxygen (Section **Fukui reactivity index calculation**).

In addition, the Hirshfeld charges of key atoms in **TS3** and **TS3a** shows that the ether oxygen atom becomes slightly positive in the **TS3a** (0.018 a.u., Supplementary Figure 8) as it attacks the iminium carbon of the Vilsmeier-Haack reagent **II**, making the transition state less favourable as a positive charge develops on oxygen atom. On the other hand, the oxetane oxygen in **TS3** has a negative charge of -0.045 a.u. (Supplementary Figure 8). HOMO and LUMO diagrams and non-covalent interactions (NCI) plots for **TS3** and **TS3a** are similar (Supplementary Figure 8).

	TS3	TS3a
Hirshfeld charges		
HOMO		

LUMO		
NCI		
	TS4	TS4a
Hirshfeld charges		

HOMO	 Diagram showing the Highest Occupied Molecular Orbital (HOMO) of the substrate molecule 8. The molecule is a long-chain structure with a phenyl ring at one end and a complex functional group at the other. The HOMO is represented by large red and blue lobes, indicating the distribution of electron density. A dashed yellow line highlights a specific interaction or bond within the molecule.	 Diagram showing the HOMO of the product molecule. The structure is similar to the substrate but with a different functional group. The HOMO is represented by large red and blue lobes, indicating the distribution of electron density. A dashed yellow line highlights a specific interaction or bond within the molecule.
LUMO	 Diagram showing the Lowest Unoccupied Molecular Orbital (LUMO) of the substrate molecule 8. The molecule is a long-chain structure with a phenyl ring at one end and a complex functional group at the other. The LUMO is represented by large red and blue lobes, indicating the distribution of electron density. A dashed yellow line highlights a specific interaction or bond within the molecule.	 Diagram showing the LUMO of the product molecule. The structure is similar to the substrate but with a different functional group. The LUMO is represented by large red and blue lobes, indicating the distribution of electron density. A dashed yellow line highlights a specific interaction or bond within the molecule.
NCI	 Diagram showing the Non-Covalent Interactions (NCI) of the substrate molecule 8. The molecule is a long-chain structure with a phenyl ring at one end and a complex functional group at the other. The NCI is represented by small red and blue lobes, indicating the distribution of non-covalent interactions. A dashed yellow line highlights a specific interaction or bond within the molecule.	 Diagram showing the NCI of the product molecule. The structure is similar to the substrate but with a different functional group. The NCI is represented by small red and blue lobes, indicating the distribution of non-covalent interactions. A dashed yellow line highlights a specific interaction or bond within the molecule.
	8 (substrate)	

Hirshfeld charges		
HOMO		
LUMO		

Supplementary Figure 8. Hirshfeld charges, frontier molecular orbitals and non-covalent interactions (NCI) plots for selected species.

Comparing the TSs for the C–Br bond formation steps (**TS4** and **TS4a**, Supplementary Figure 8), the frontier molecular orbitals (FMOs) are also similar, and NCI plots seem to suggest that the NCIs in **TS4a** may be more favourable. Despite these, reaction via

TS4 has a much lower barrier (1.7 kcal/mol from the complex preceding the TS) than that via **TS4a** (7.4 kcal/mol from the complex preceding the TS), likely because the release of oxetane ring strain in **TS4** contributes to lowering the barrier. To summarize, the steps for reaction with the Vilsmeier-Haack reagent **II** and subsequent C–Br bond formation are both energetically more favourable for the oxetane oxygen compared to the ether oxygen, as a consequence of the greater nucleophilicity of the oxetane oxygen and release of ring strain during C–Br formation.

Simple transition state theory (TST) for rate estimation

The barrier difference $\Delta\Delta G^\ddagger$ between two transition states can be used to predict the kinetic preference for the major pathway over the minor pathway, using simple transition state theory as an estimate and without Boltzmann weighting of all the conformers.

The Eyring equation

$$k = \frac{k_B T}{h} e^{-\Delta G^\ddagger / RT}$$

gives the rate constant under simple transition state theory (TST) assumptions.

Under kinetic control, as we compare the barrier heights difference between competing transition states, the ratio of the rates between two pathways is given by:

$$\frac{k_A}{k_B} = \frac{e^{-\Delta G_A^\ddagger / RT}}{e^{-\Delta G_B^\ddagger / RT}} = e^{-\Delta\Delta G^\ddagger / RT}$$

where k_X is the rate constant of pathway X (X=A or B); $\Delta G_X^\ddagger$ is the activation barrier for pathway X; and $\Delta\Delta G_X^\ddagger$ is the difference in the barrier heights; and R is the gas constant, T the temperature. Note that the Eyring Equation pre-exponential factor cancels when comparing the ratio of the rate constants. Thus, using the calculated $\Delta\Delta G_X^\ddagger$ value (difference of barrier heights between competing TSs) at the reaction temperature (e.g., 25°C = 298.15K), we are able to obtain the ratio of competing rates.

Fukui reactivity index calculation

To quantify which of the oxygen atoms (oxetane oxygen or acyclic ether oxygen) in substrate **8** is more nucleophilic, we calculated the local Fukui reactivity index at each site. The Fukui index for electrophilic attack (as a nucleophile) at molecular site k is given by⁴¹

$$f_k^- = q_k(N) - q_k(N-1)$$

where $q_k(N)$ is the charge of the neutral system (with N electrons) at site k and $q_k(N-1)$ is the charge of the radical cationic system (with $N-1$ electrons) at site k .

Using the SMD(DMF)-M06-2X/def2-SVP optimized geometry, we computed single point Hirshfeld charges of both the neutral and radical cationic systems of the substrate at the same geometry and obtained the Fukui index for electrophilic attack at oxetane oxygen as 0.322 a.u. and at ether oxygen as 0.006 a.u., showing that the oxetane oxygen is much more nucleophilic (more prone to electrophilic attack) than the ether oxygen.

Optimised structures and absolute energies

Geometries of all optimised structures (in .xyz format with their associated gas-phase energy in Hartrees) are included in a separate folder named *DFT_optimised_structures* with an associated readme.txt file. All these data have been uploaded to zenodo.org (DOI: [10.5281/zenodo.14538630](https://doi.org/10.5281/zenodo.14538630)).

Absolute values (in Hartrees) for SCF energy, zero-point vibrational energy (ZPE), enthalpy and quasi-harmonic Gibbs free energy (at 25°C/298.15 K) for optimized structures are given below. Single point corrections in SMD DMF using M06-2X/BS2 level of theory are also included.

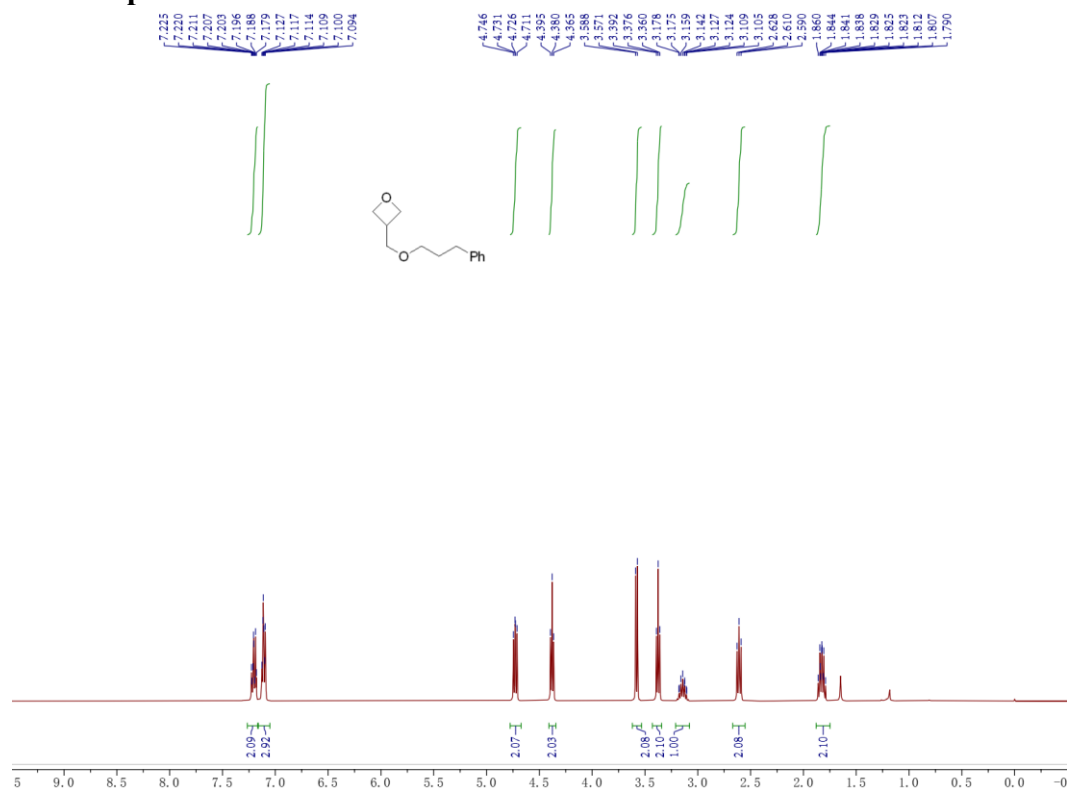
Structure	E/au	ZPE/au	H/au	T.S/au	qh-G/au	SP
substrate	-655.849811	0.288525	-655.54566	0.057971	-655.599971	-656.5926142
bromide	-2574.059928	0	-2574.0576	0.015517	-2574.073085	-2574.363403
Br2CO	-5260.975548	0.00971	-5260.9606	0.032407	-5260.992996	-5261.72158
DMF	-248.216806	0.103124	-248.10669	0.033031	-248.13966	-248.5070715

I	-10581.82101	0.114198	-10581.692	0.057179	-10581.74653	-10583.36853
TS1	-10581.82046	0.113563	-10581.693	0.055025	-10581.74574	-10583.36754
INT1	-10581.82104	0.11363	-10581.693	0.055659	-10581.74653	-10583.36832
TS2	-10581.80571	0.111995	-10581.68	0.054286	-10581.73241	-10583.35336
INT2	-10581.81965	0.112284	-10581.691	0.064122	-10581.74973	-10583.37052
II	-2746.772993	0.101125	-2746.6645	0.035584	-2746.699913	-2747.277628
INT3	-3402.635749	0.391366	-3402.2206	0.079893	-3402.293186	-3403.878769
TS3	-3402.625902	0.391533	-3402.2116	0.077724	-3402.282416	-3403.86446
III	-5976.704955	0.393473	-5976.2864	0.082751	-5976.362044	-5978.246531
TS4	-5976.700197	0.391769	-5976.2835	0.08305	-5976.359241	-5978.241997
IV	-5976.789361	0.39466	-5976.3694	0.08376	-5976.445347	-5978.329091
TS5	-5976.742723	0.391524	-5976.3262	0.08181	-5976.40119	-5978.286705
INT4	-5976.780723	0.391324	-5976.3636	0.083538	-5976.440136	-5978.327927
V	-5728.548621	0.286773	-5728.2436	0.066218	-5728.305158	-5729.809409
INT3b	-11237.67967	0.403851	-11237.244	0.101	-11237.33455	-11239.96411
TS3b	-11237.66762	0.404489	-11237.233	0.096893	-11237.32021	-11239.94996
VI	-11237.66806	0.405202	-11237.232	0.097986	-11237.32029	-11239.94955
TS4b	-11237.66183	0.403707	-11237.228	0.096297	-11237.31485	-11239.94394
INT4b	-11237.73213	0.405147	-11237.297	0.094309	-11237.3826	-11240.01287
INT3a	-3402.63328	0.391475	-3402.218	0.078755	-3402.289811	-3403.876437
TS3a	-3402.614125	0.393729	-3402.1985	0.072125	-3402.265754	-3403.852109
VIII	-5976.687681	0.394564	-5976.2681	0.082211	-5976.343059	-5978.229323
TS4a	-5976.672982	0.392213	-5976.2559	0.0814	-5976.330526	-5978.215335
INT4a	-5976.736987	0.392593	-5976.3182	0.088127	-5976.396784	-5978.282131
TS4a'	-5976.674673	0.392427	-5976.2578	0.078444	-5976.330744	-5978.214821
IX	-2805.437679	0.106926	-2805.3234	0.037042	-2805.359594	-2806.011864
X	-3171.293752	0.284973	-3170.9911	0.063453	-3171.050186	-3172.266406
TS5a	-3171.252926	0.281628	-3170.9536	0.063791	-3171.012773	-3172.228764
INT5a	-3171.297587	0.281546	-3170.9977	0.064667	-3171.057928	-3172.275704

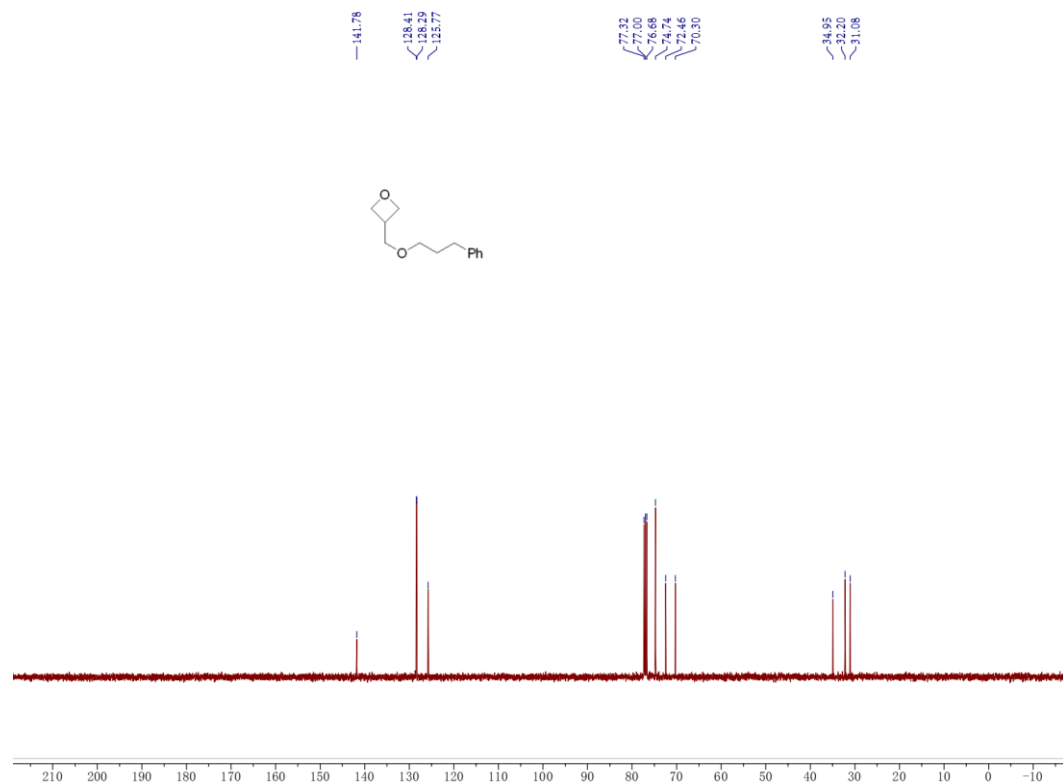
XI	-2923.071955	0.177104	-2922.8842	0.046171	-2922.928233	-2923.762819
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7. NMR Spectra

^1H NMR spectrum of 8



^{13}C NMR spectrum of 8



Chemical structure of 1-(4-oxaspiro[3.3]hept-2-yl)propyl phenyl ether:

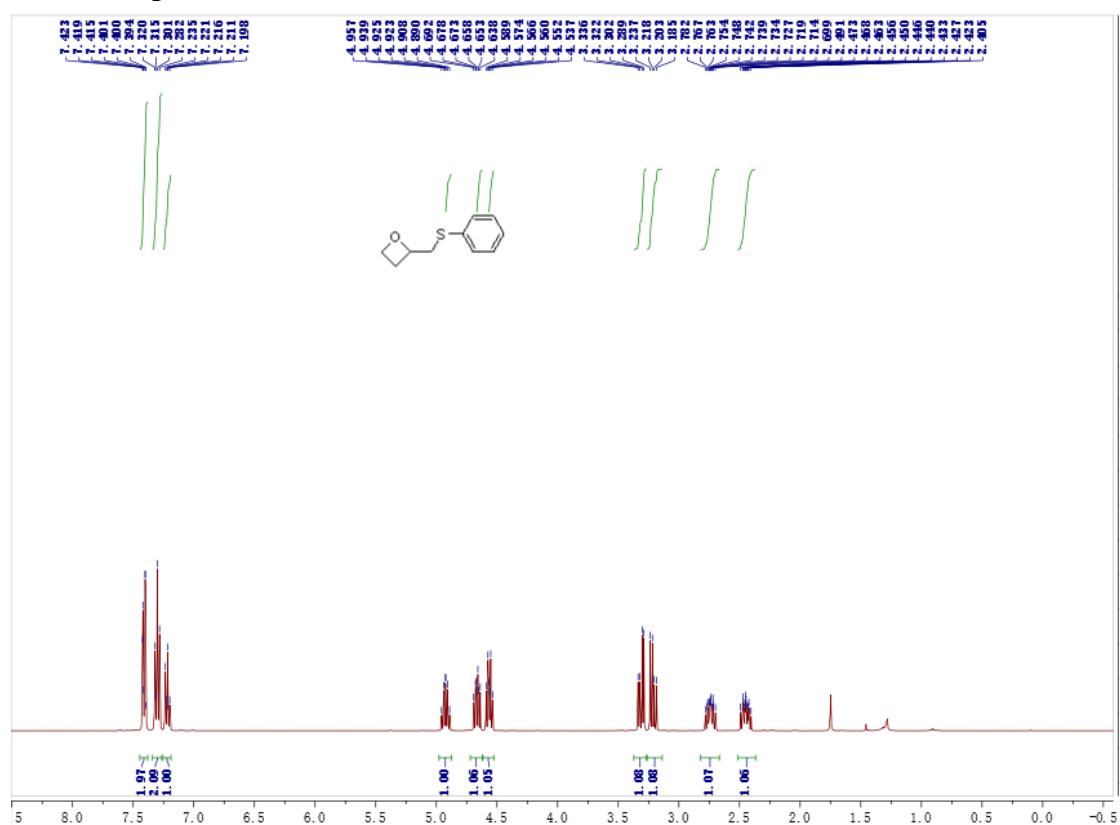
C1CC2OC1CCC2OCCc3ccccc3

¹³C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

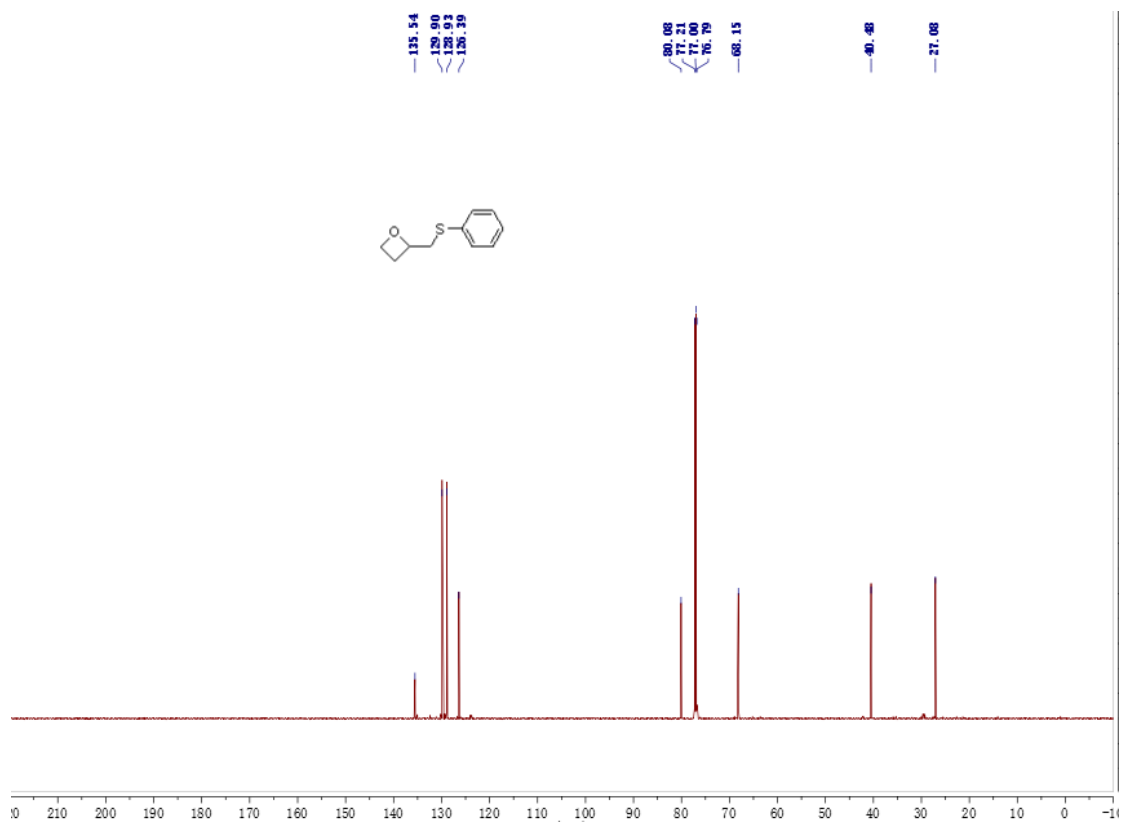
- 141.06
- 128.45
- 128.29
- 126.73
- 81.17
- 77.32
- 77.00
- 76.68
- 74.18
- 70.81
- 68.51
- 32.26
- 31.27
- 23.80

The spectrum displays a complex set of peaks, including aromatic signals between 126-141 ppm, a solvent triplet at 77 ppm, and aliphatic signals between 24-81 ppm.

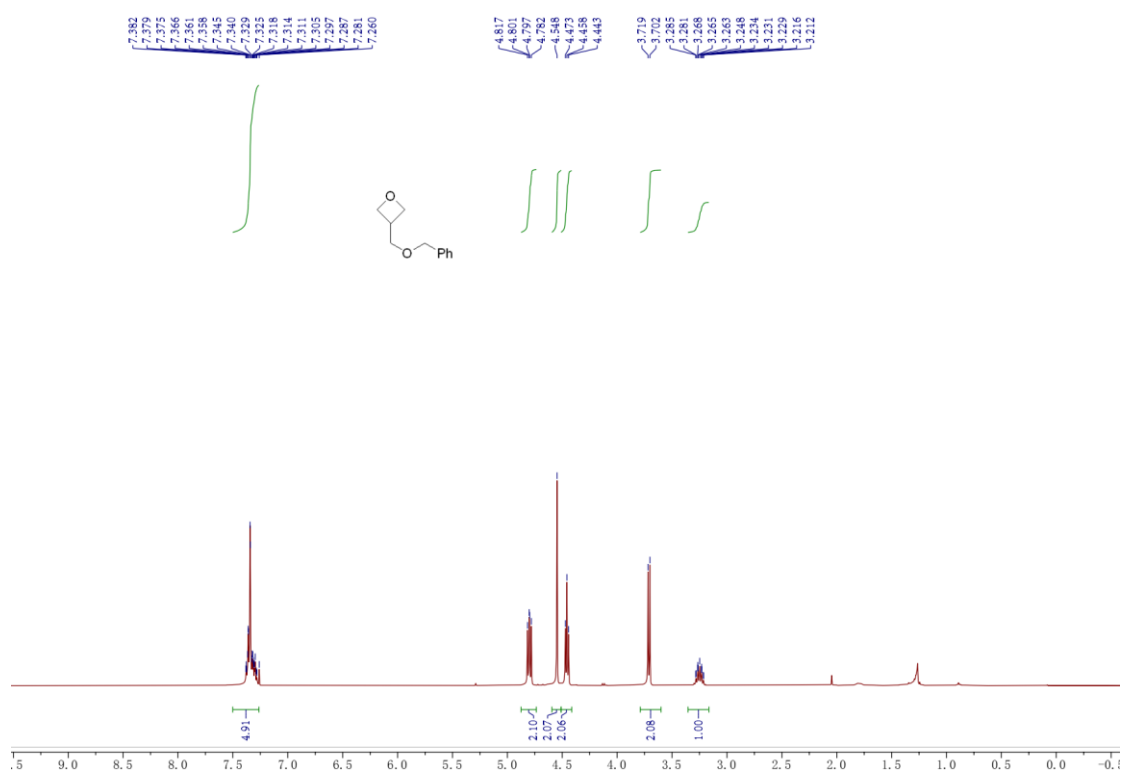
¹H NMR spectrum of S2



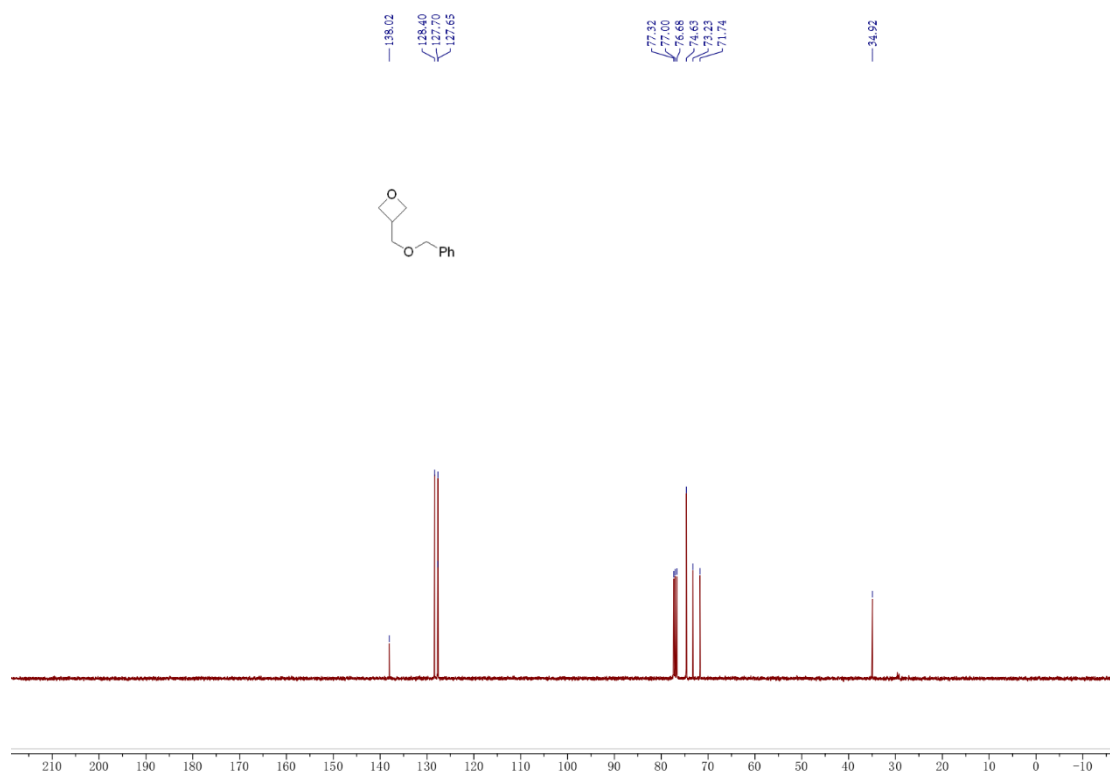
¹³C NMR spectrum of S2



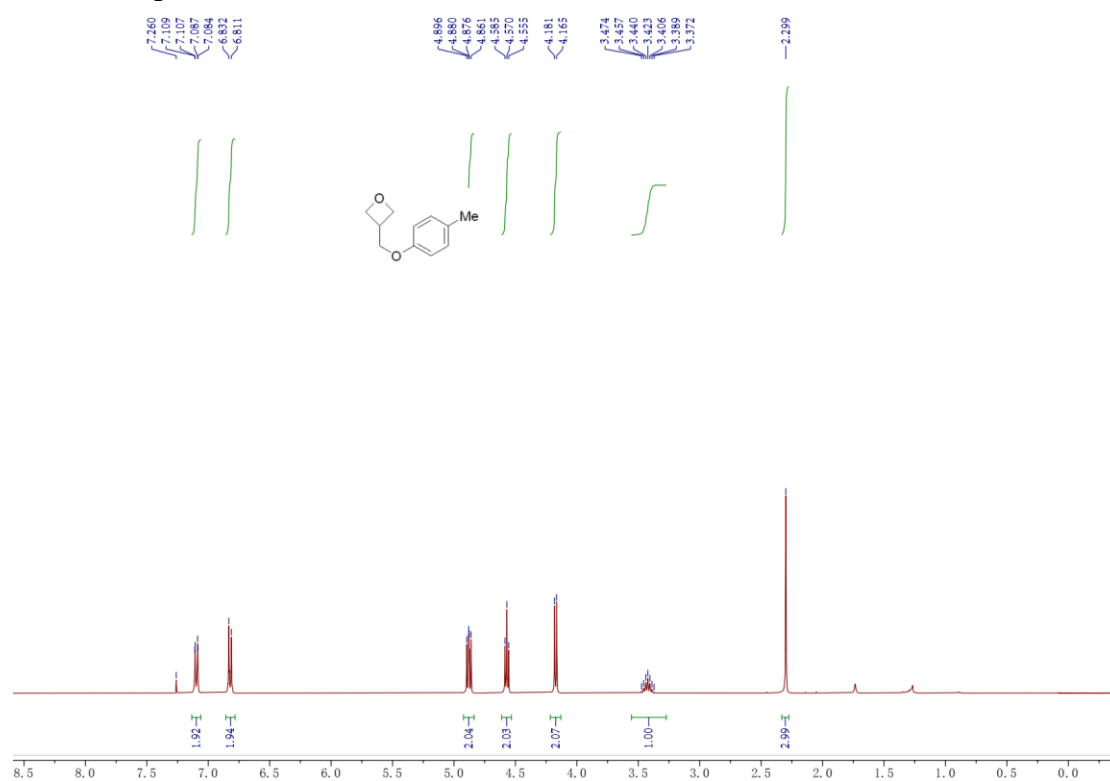
¹H NMR spectrum of S3



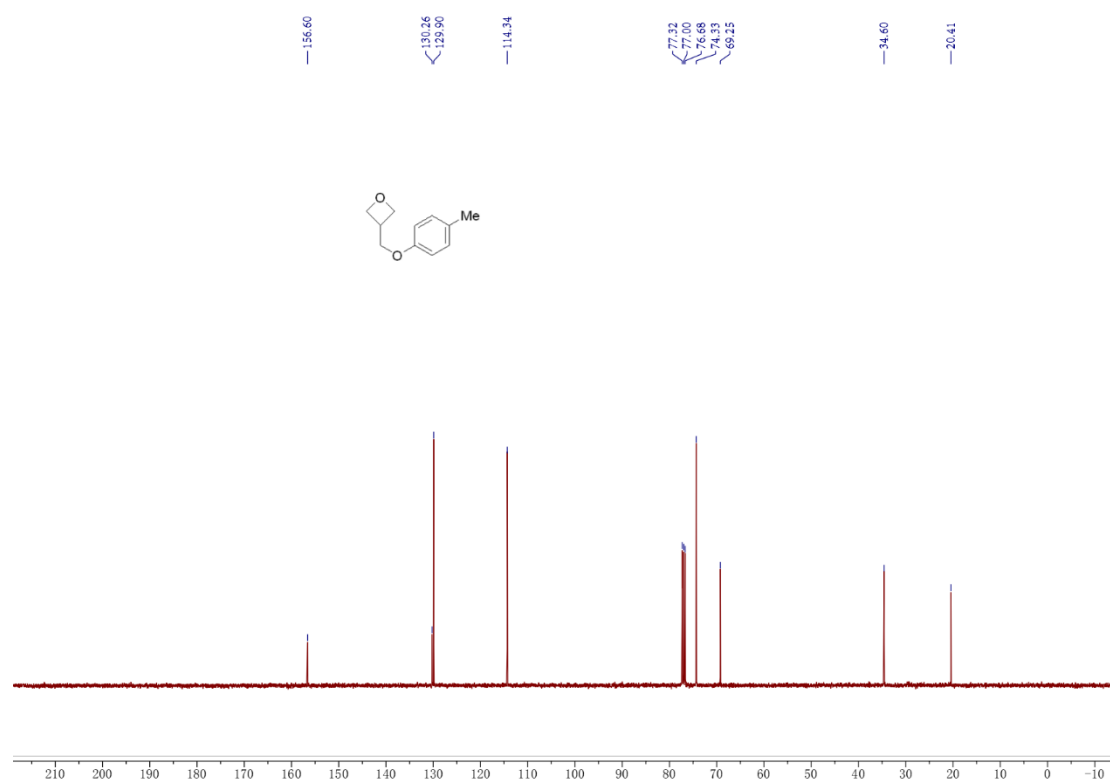
¹³C NMR spectrum of S3



¹H NMR spectrum of S4



¹³C NMR spectrum of S4



Chemical structure: C1COCC1c2ccccc2F

¹H NMR spectrum (CDCl₃) data:

Chemical Shift (ppm)	Integration
7.260, 7.255, 7.235, 7.238, 7.235, 7.217, 7.244, 7.197, 7.173, 7.171, 6.705, 6.709, 6.703, 6.697, 6.695, 6.691, 6.689, 6.684, 6.682, 6.687, 6.677, 6.675, 6.671, 6.668, 6.656, 6.654, 6.649, 6.642, 6.636, 6.631, 6.615, 6.609, 4.894, 4.878, 4.874, 4.858, 4.573, 4.558, 4.543, 4.179, 3.183, 3.163, 3.159, 3.156, 3.444, 3.442, 3.439, 3.430, 3.427, 3.425, 3.422, 3.400, 3.410, 3.408, 3.405, 3.393, 3.391, 3.388	1.01, 2.99, 1.96, 1.99, 2.01, 1.00

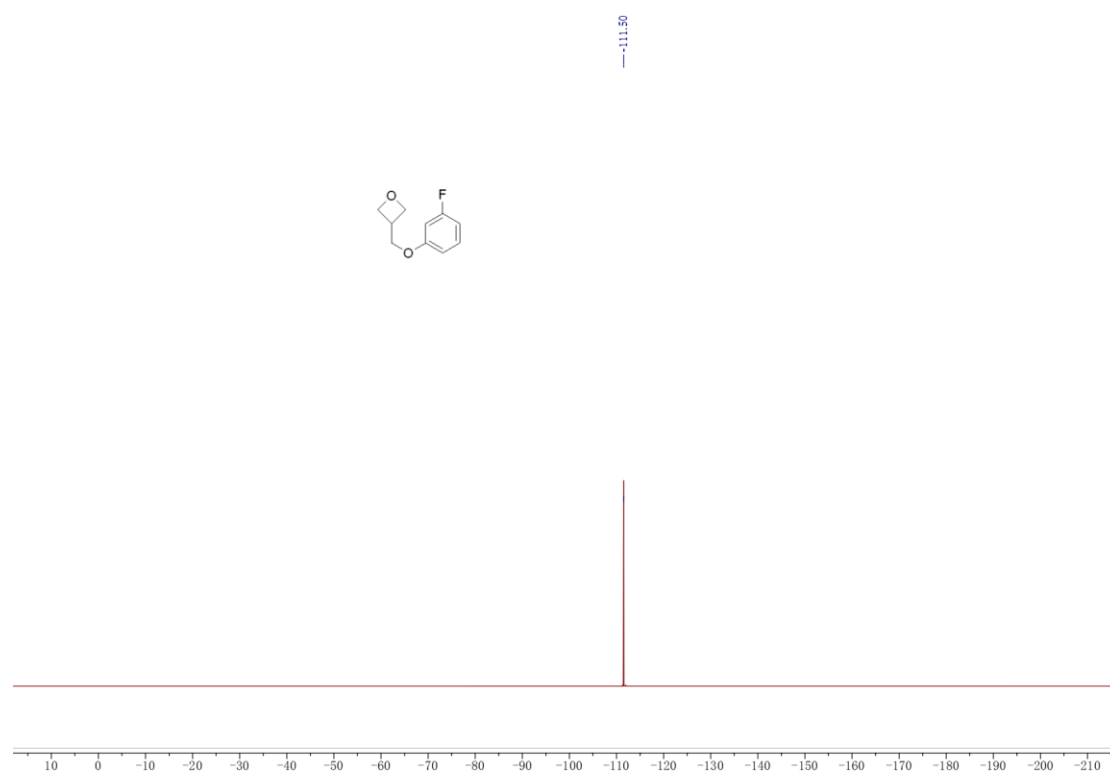
Chemical structure: Fc1ccc(cc1)C2OCCO2

¹³C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

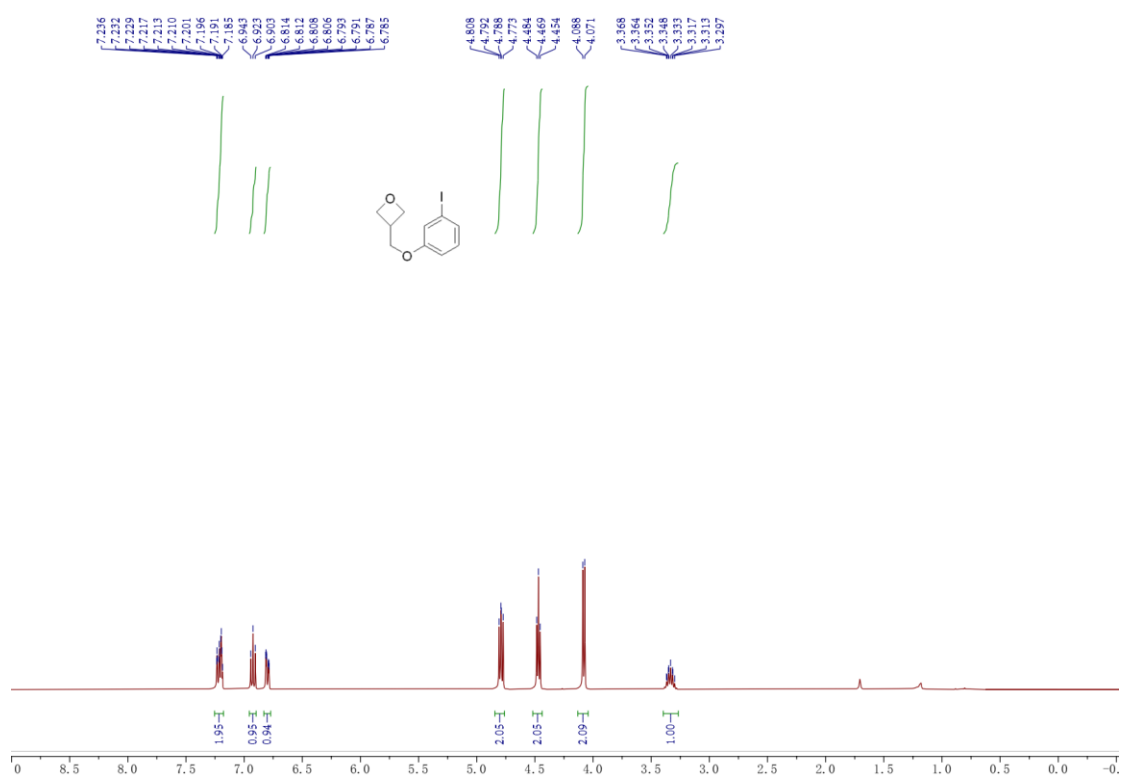
- 164.79
- 162.16
- 159.99
- 130.29
- 130.18
- 110.21
- 110.18
- 107.91
- 107.70
- 102.33
- 102.08
- 77.32
- 77.00
- 76.68
- 76.41
- 69.46
- 34.42

Chemical structure: Fc1ccc(cc1)C2OCCO2

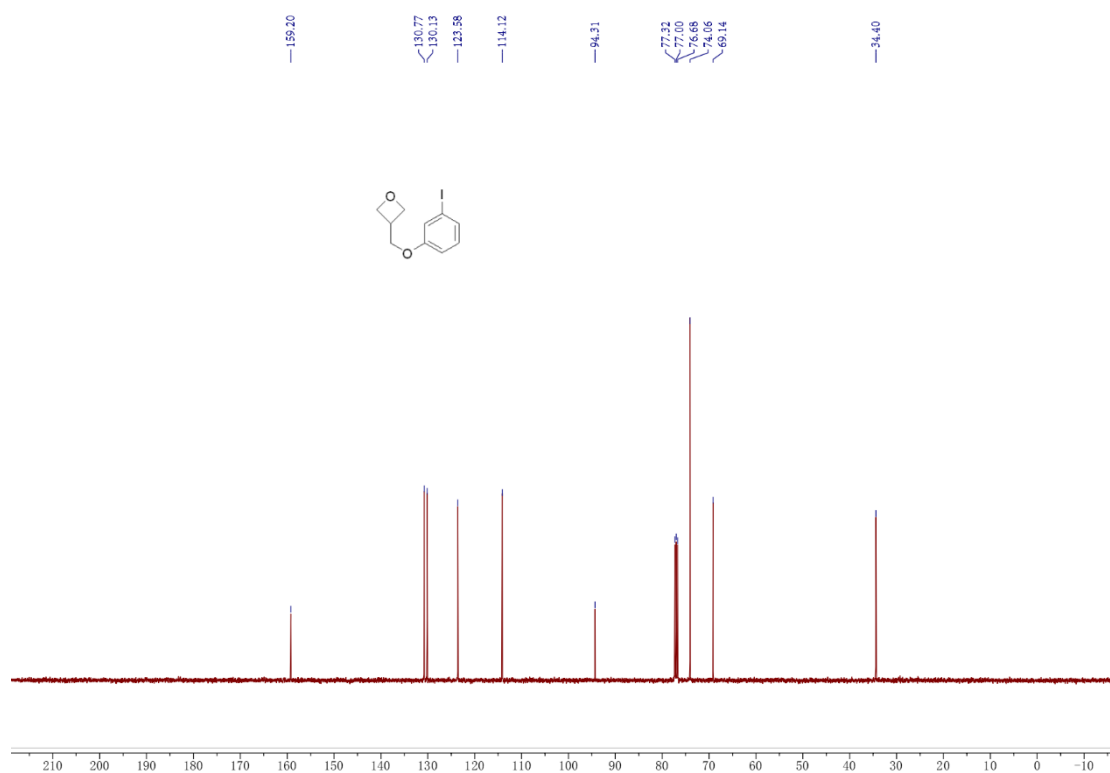
^{19}F NMR spectrum of S5



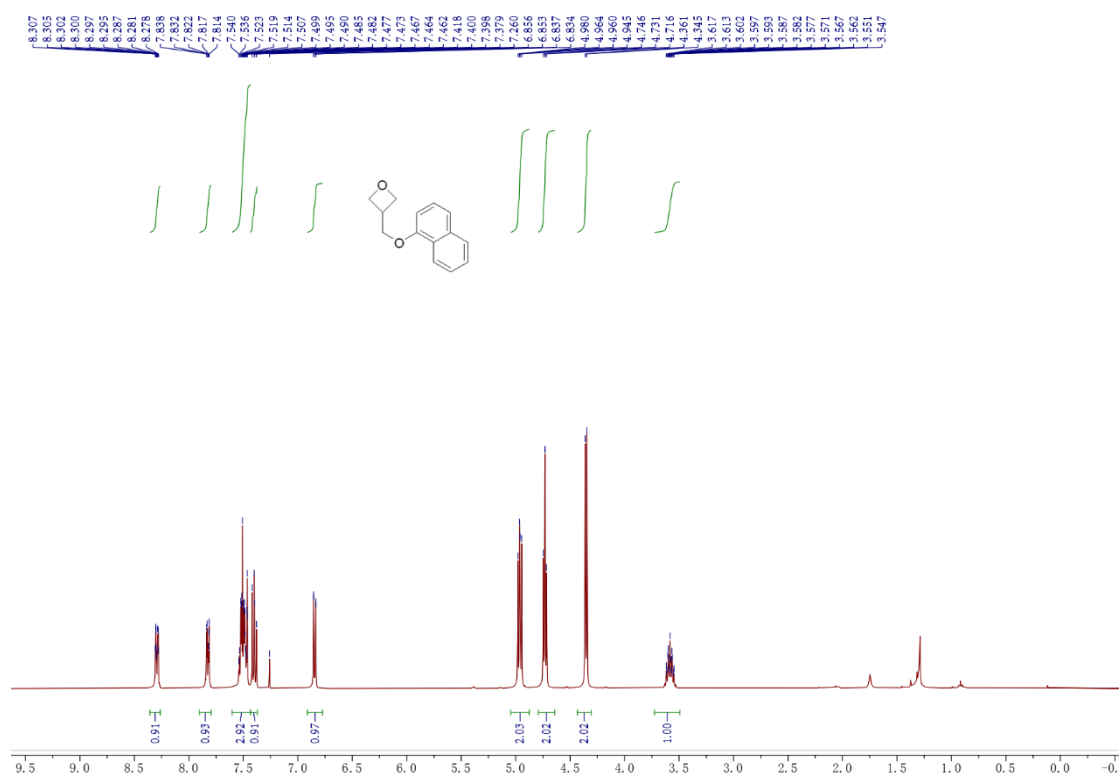
¹H NMR spectrum of S6



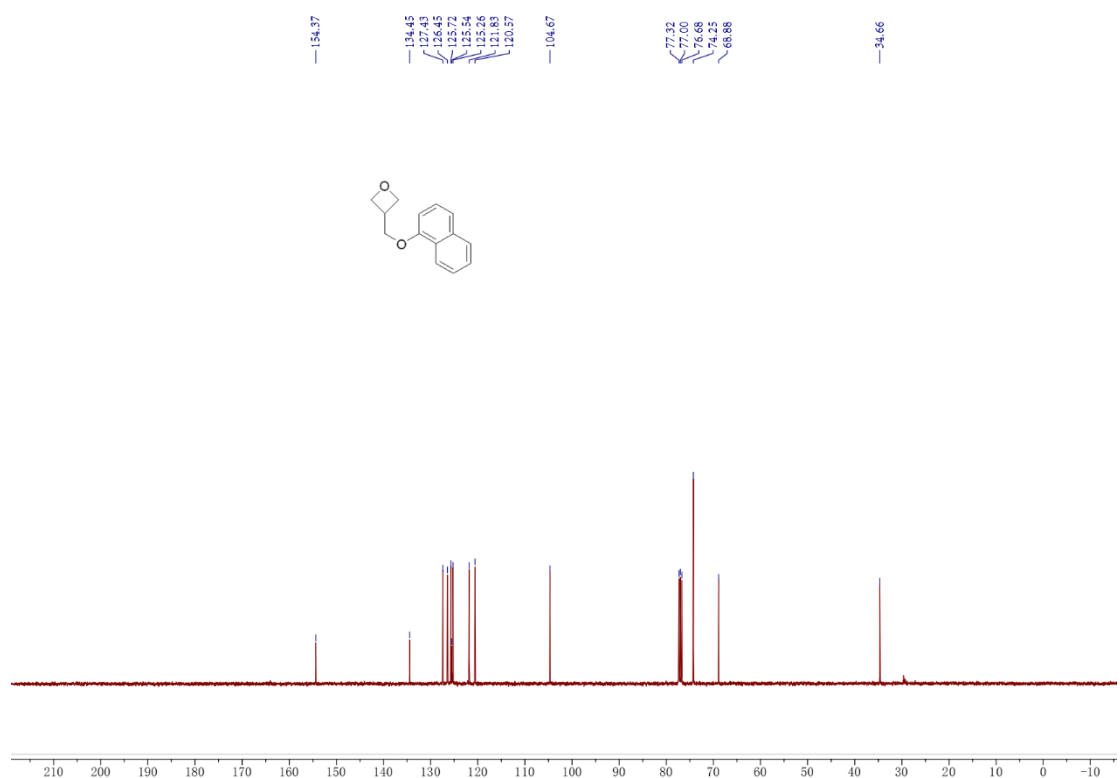
¹³C NMR spectrum of S6



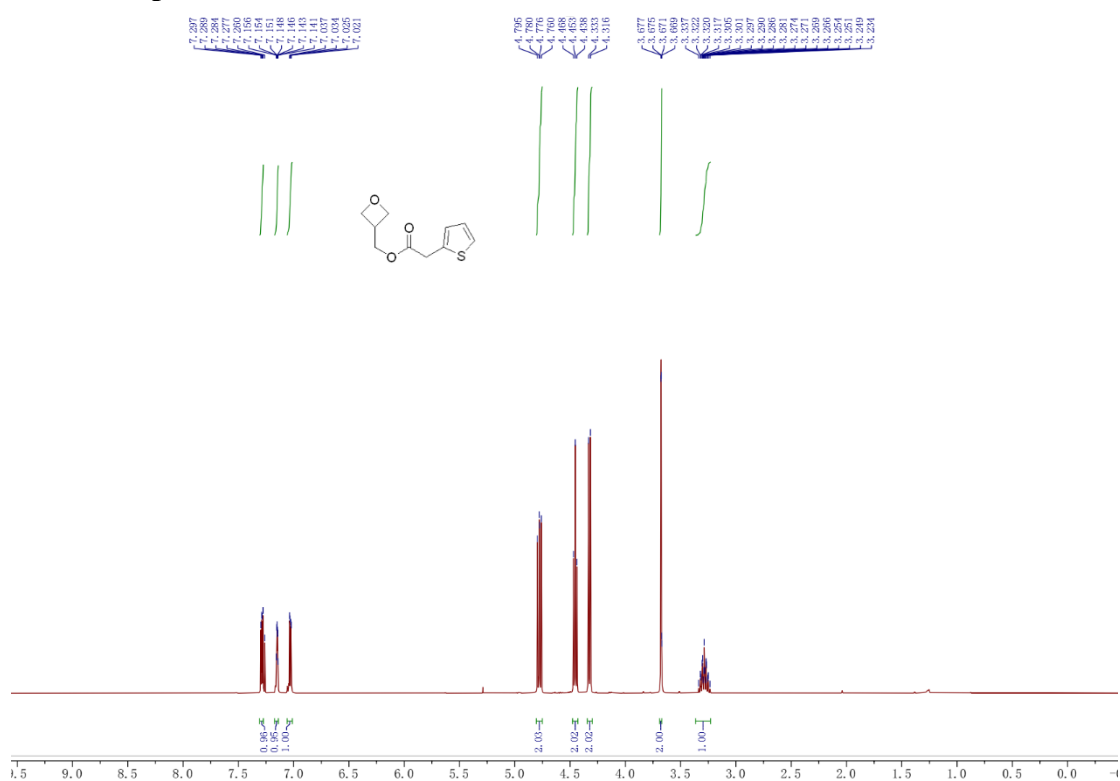
¹H NMR spectrum of S7



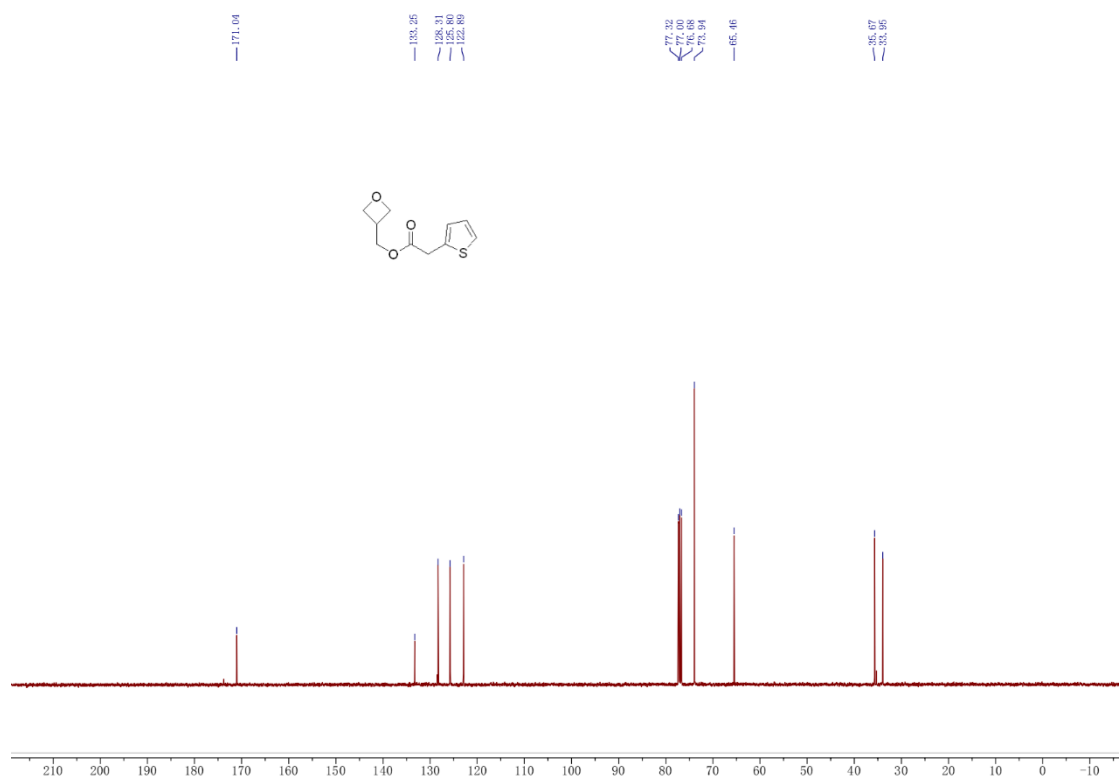
¹³C NMR spectrum of S7



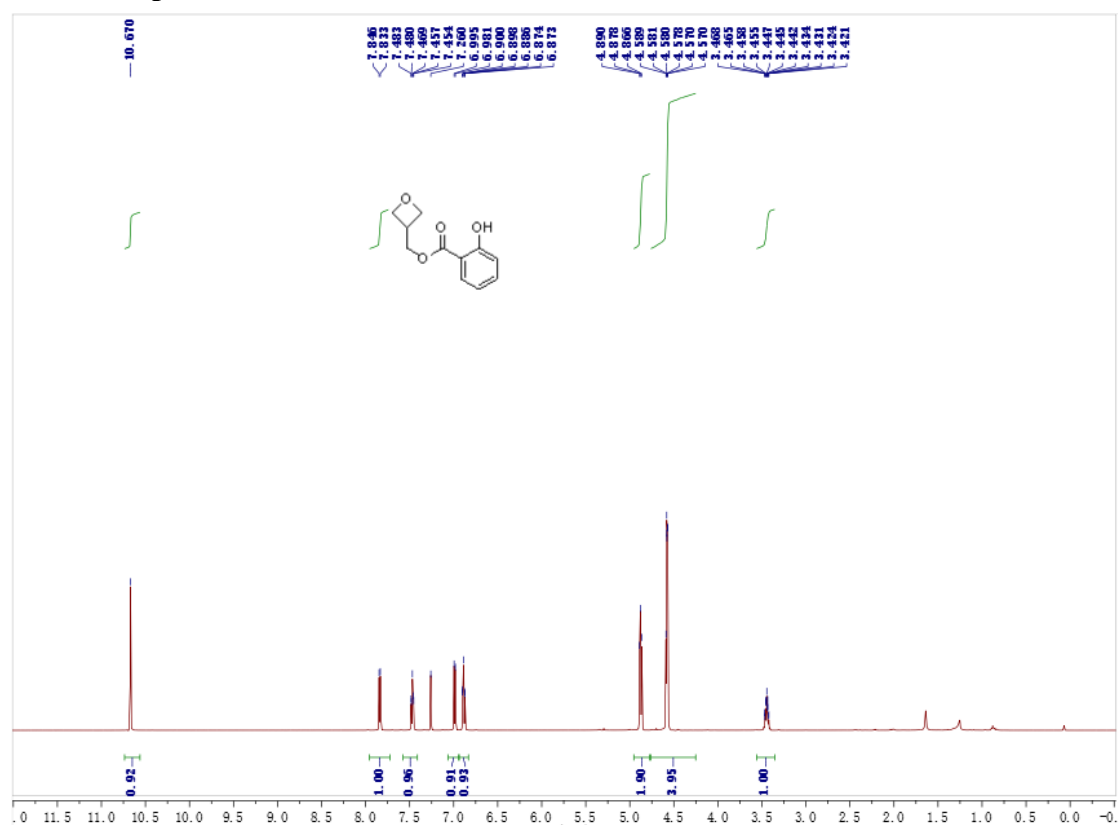
¹H NMR spectrum of S8



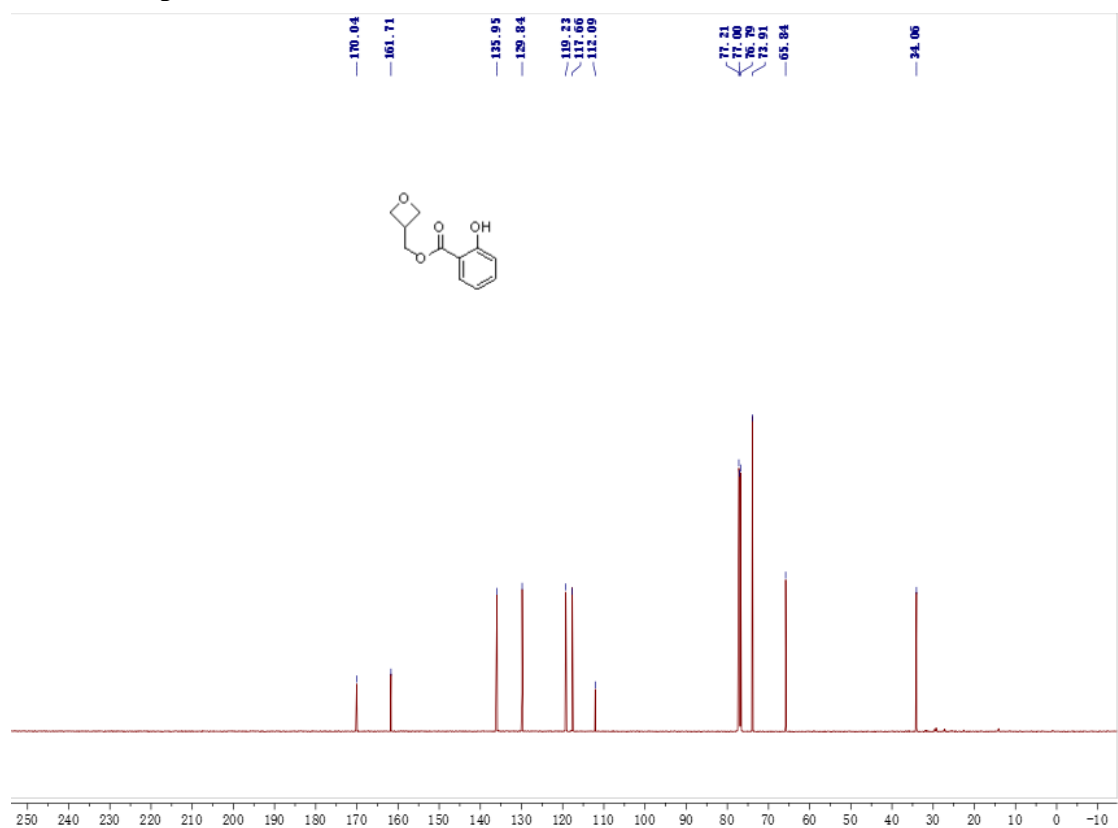
¹³C NMR spectrum of S8



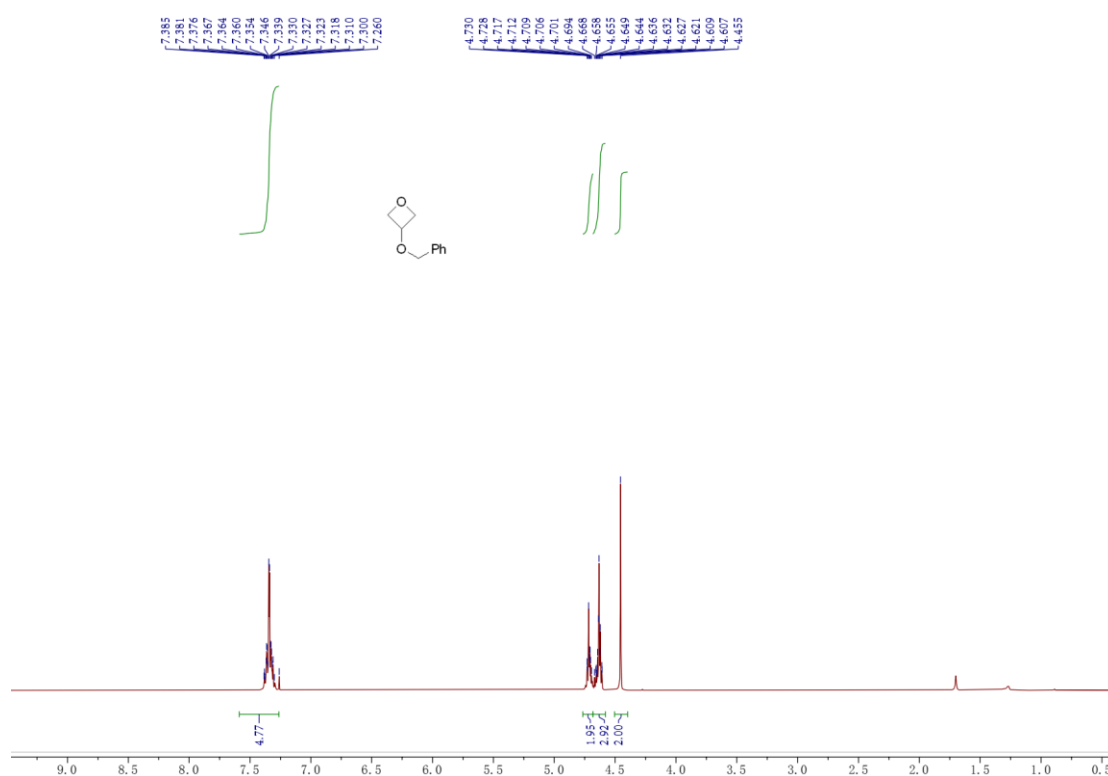
¹H NMR spectrum of S9



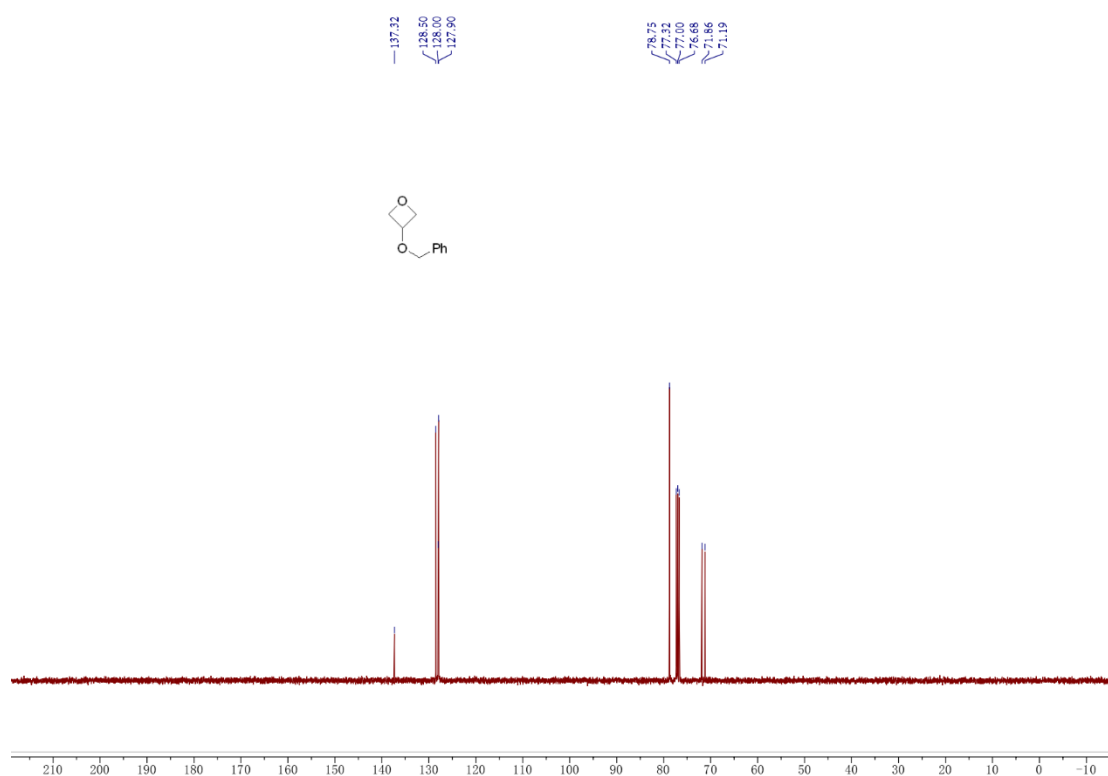
¹³C NMR spectrum of S9



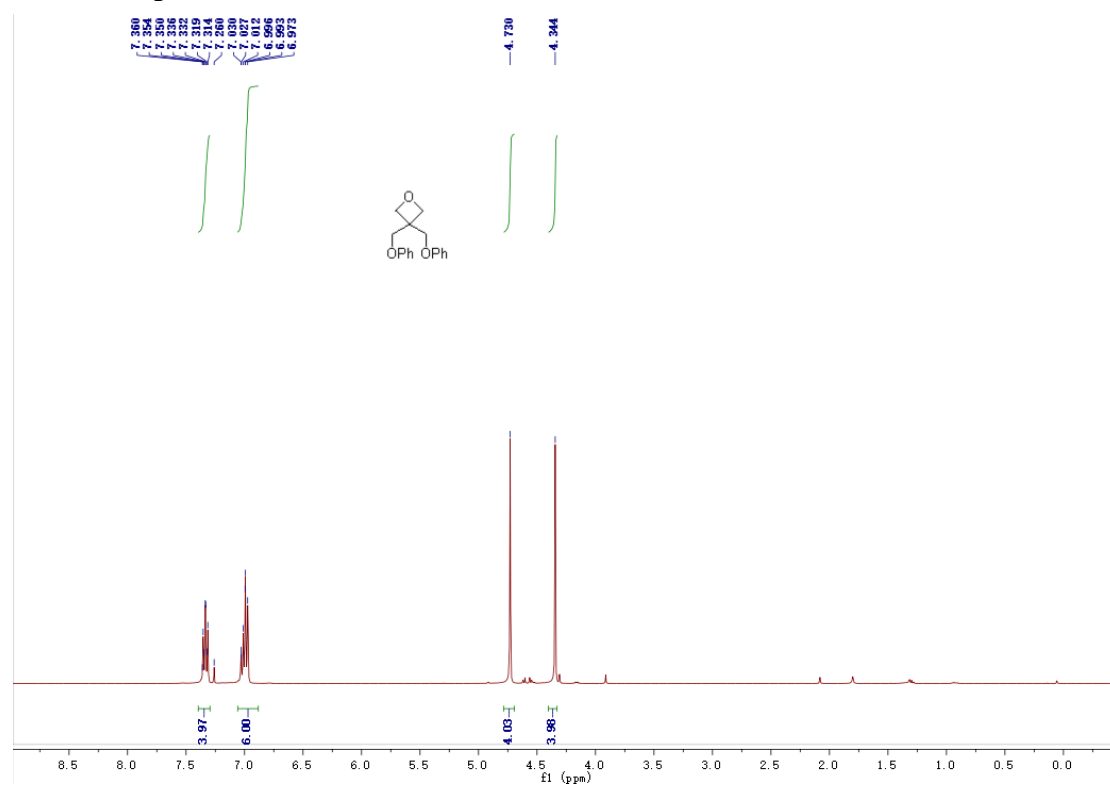
¹H NMR spectrum of S10



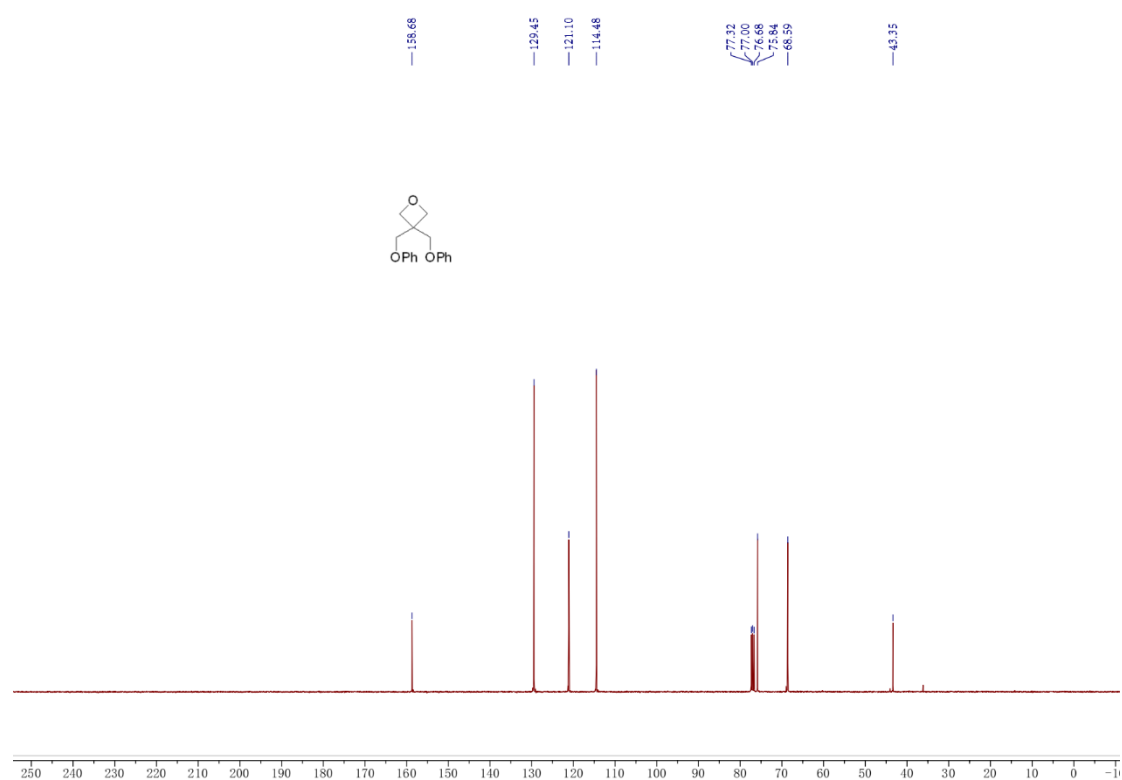
¹³C NMR spectrum of S10



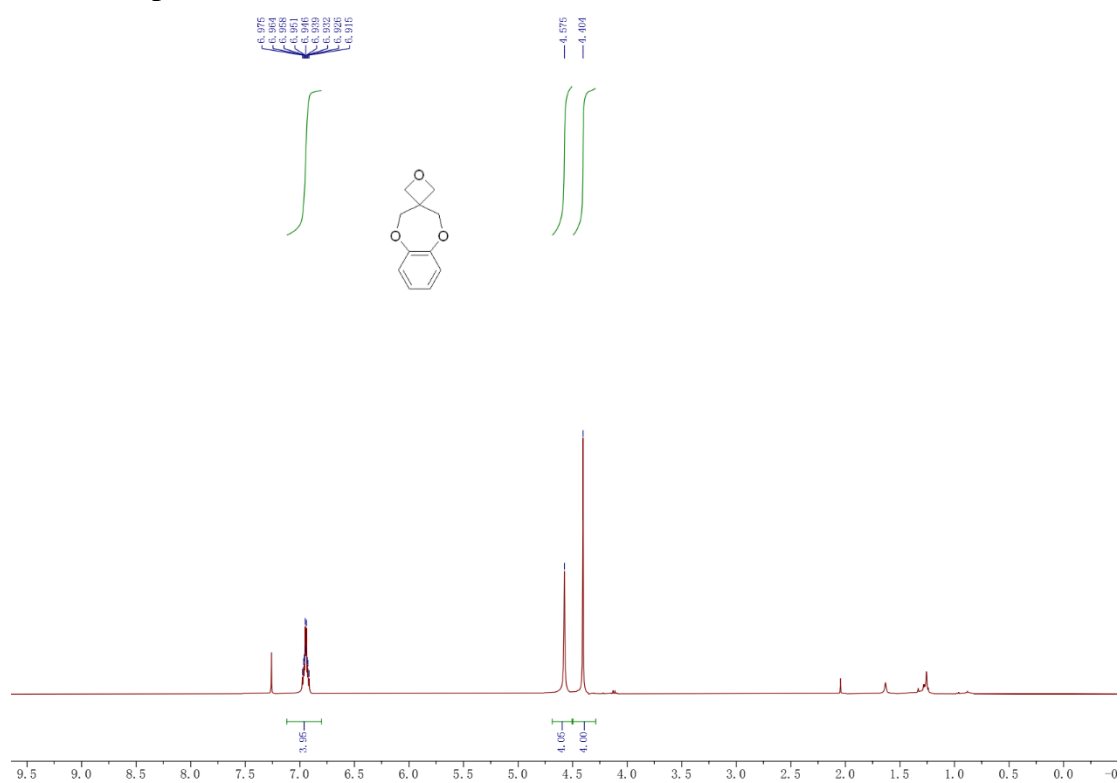
¹H NMR spectrum of S11



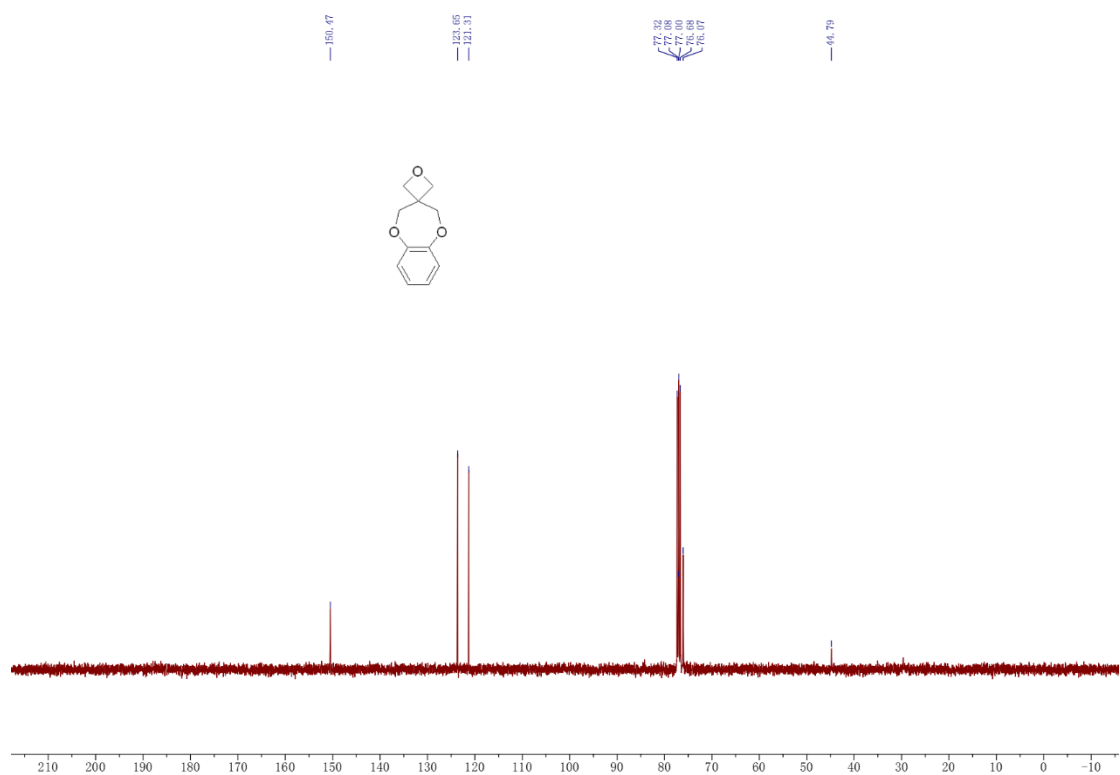
¹³C NMR spectrum of S11



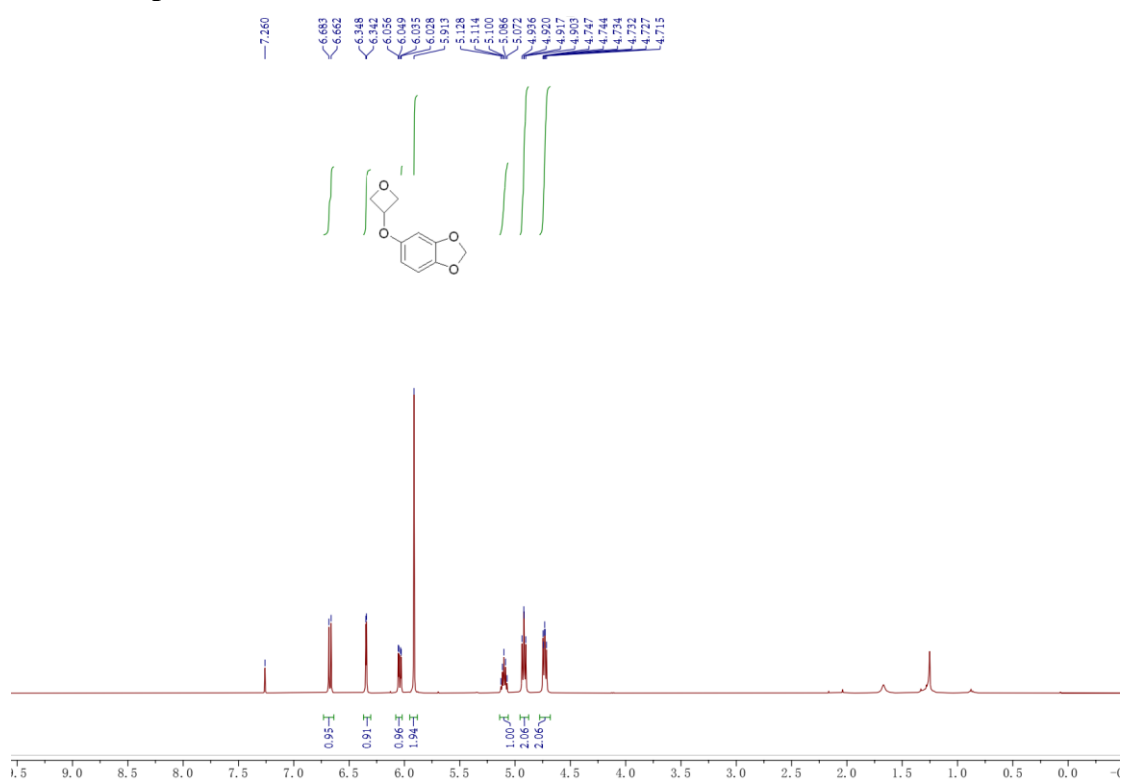
¹H NMR spectrum of 65



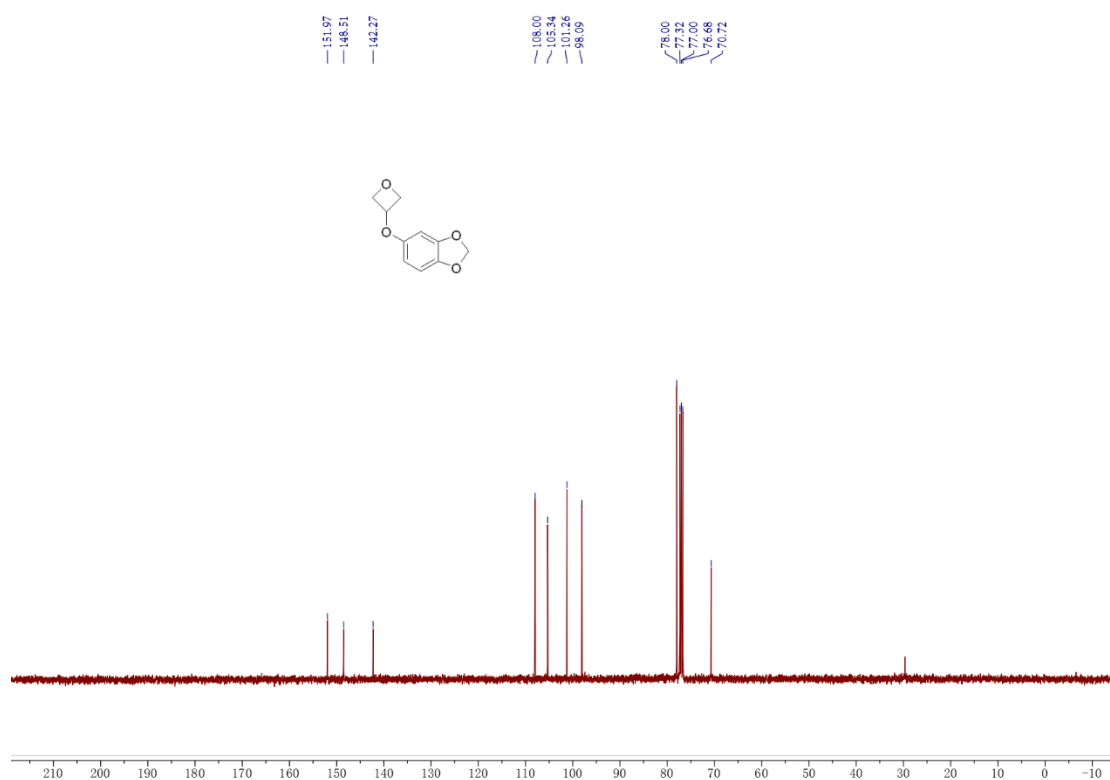
¹³C NMR spectrum of 65



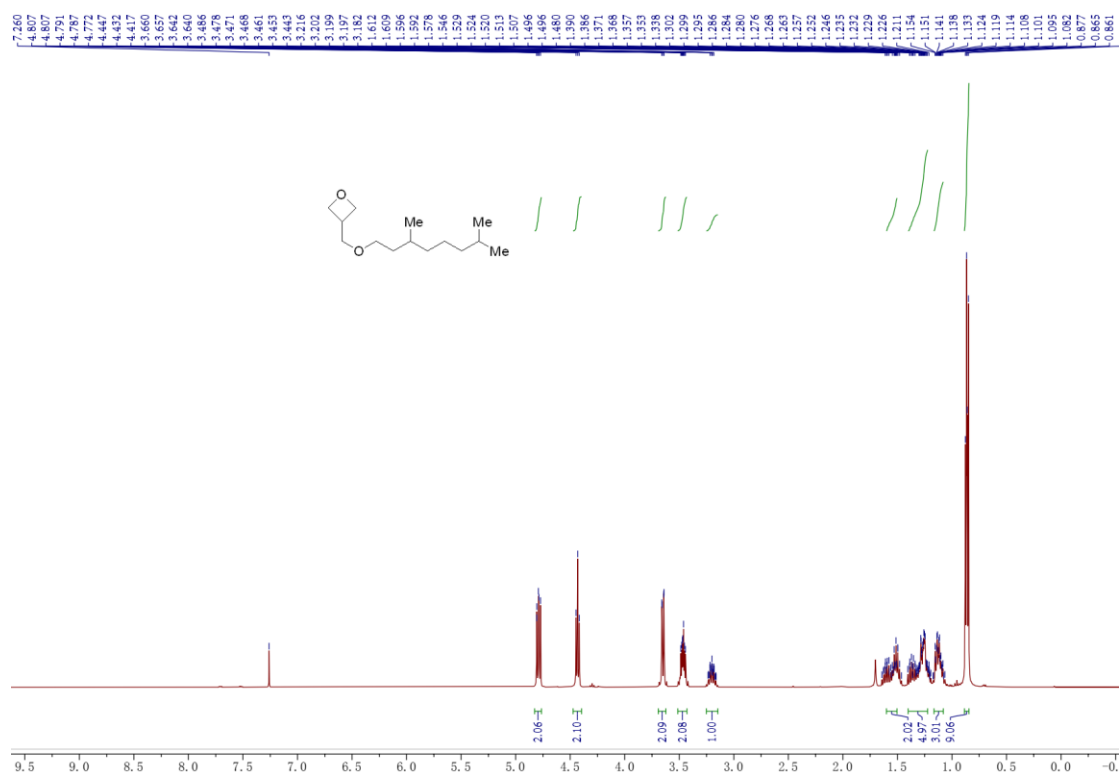
¹H NMR spectrum of S12



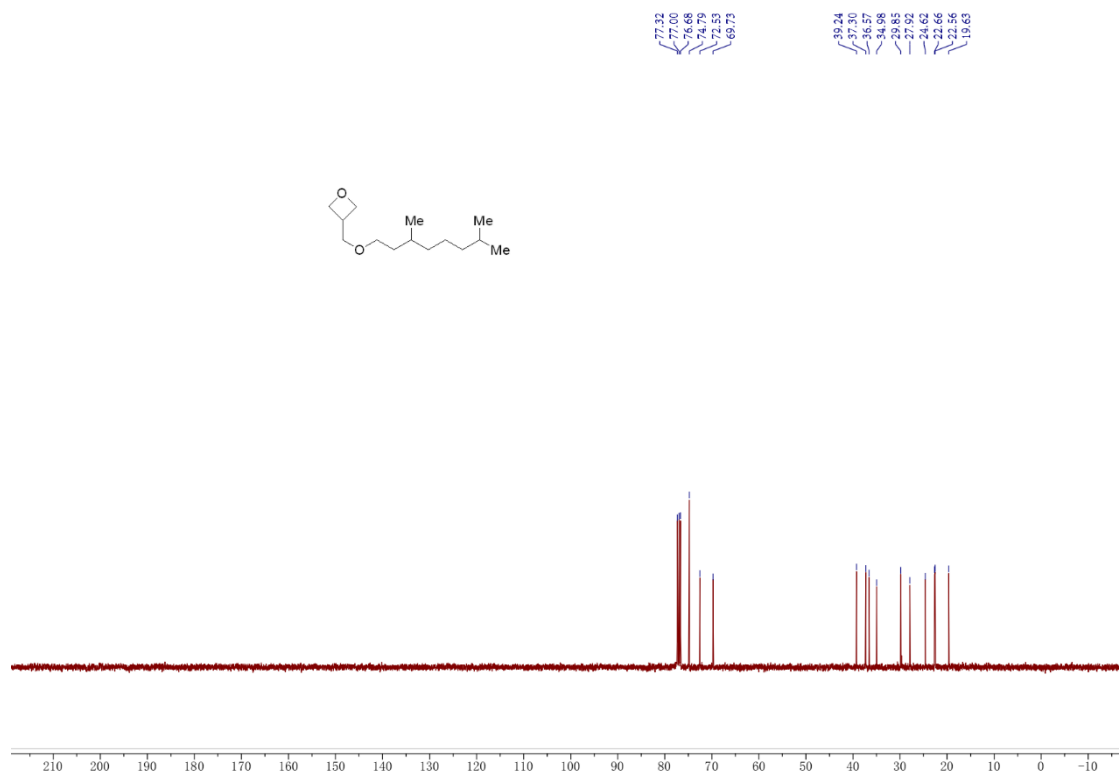
¹³C NMR spectrum of S12



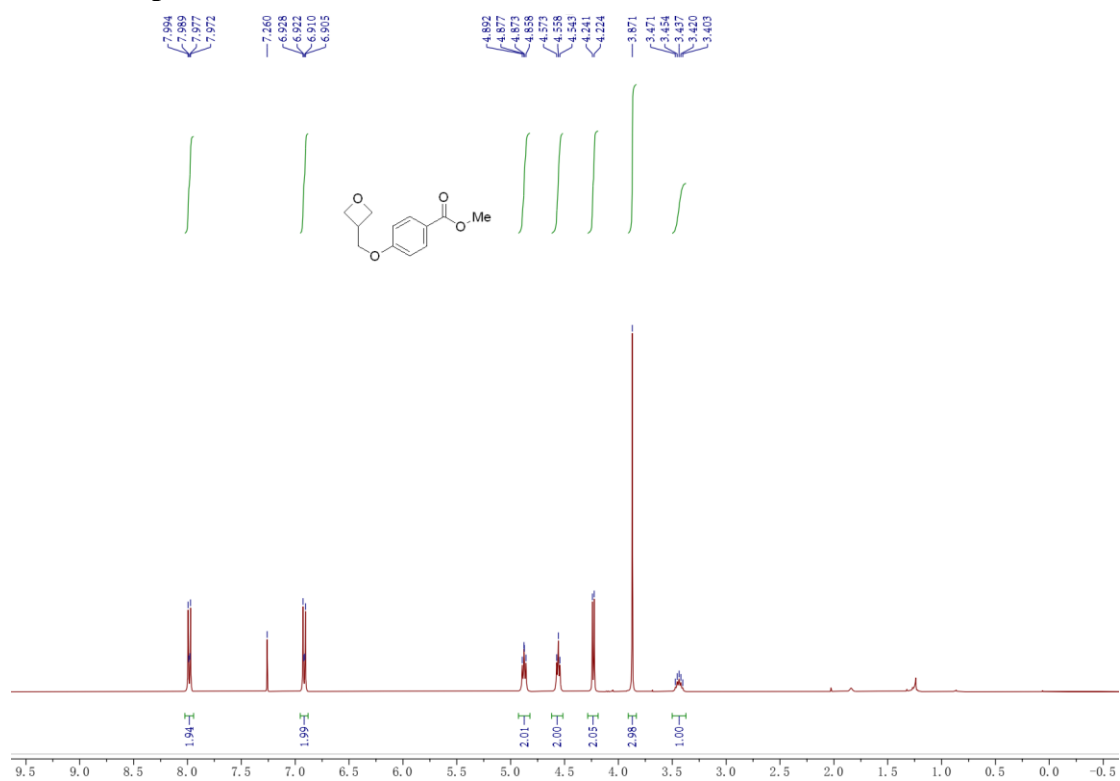
¹H NMR spectrum of S13



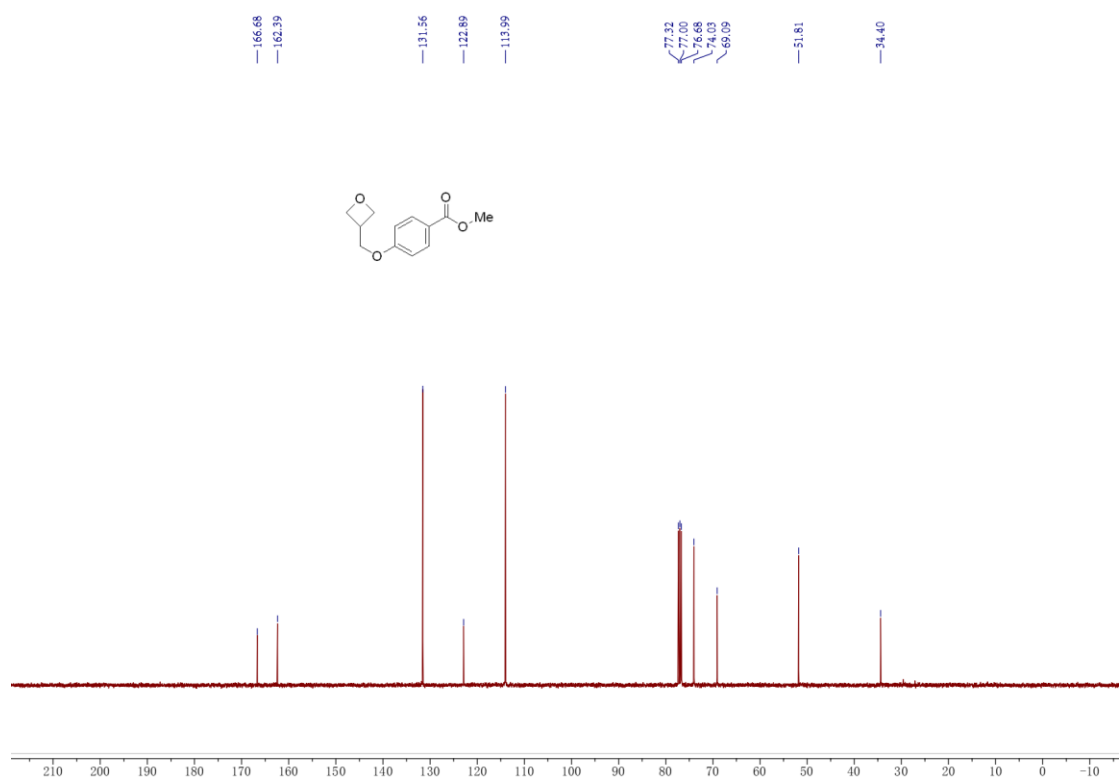
¹³C NMR spectrum of S13



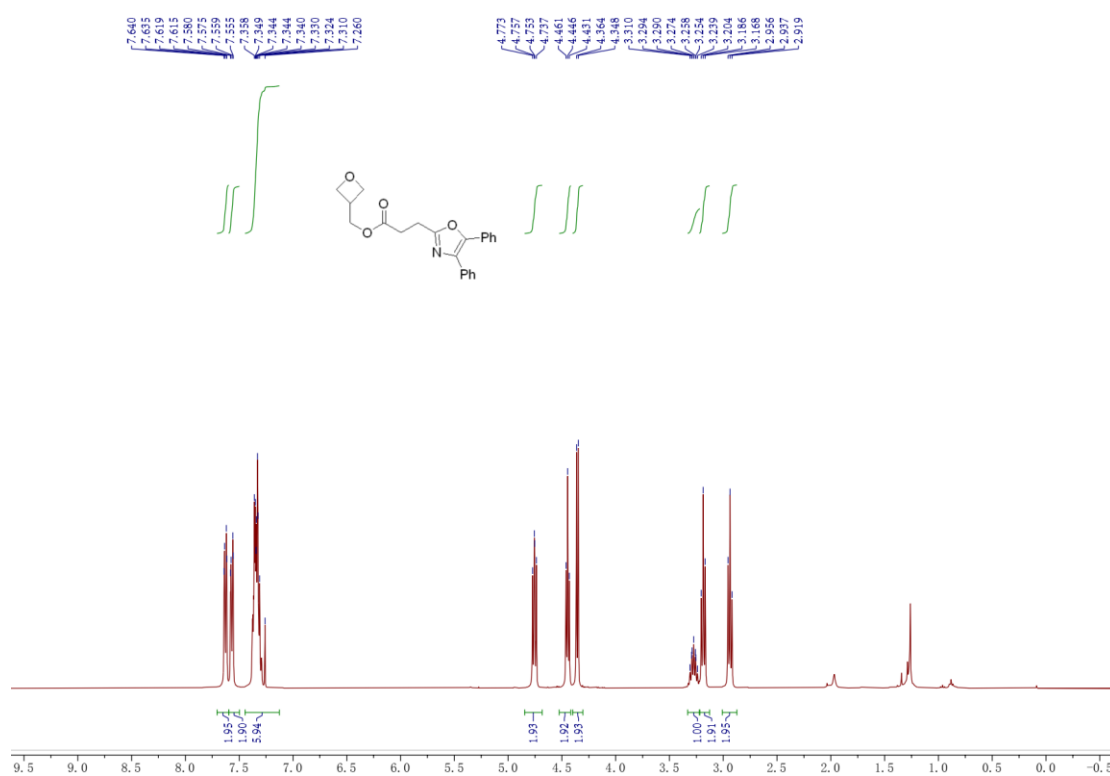
¹H NMR spectrum of S14



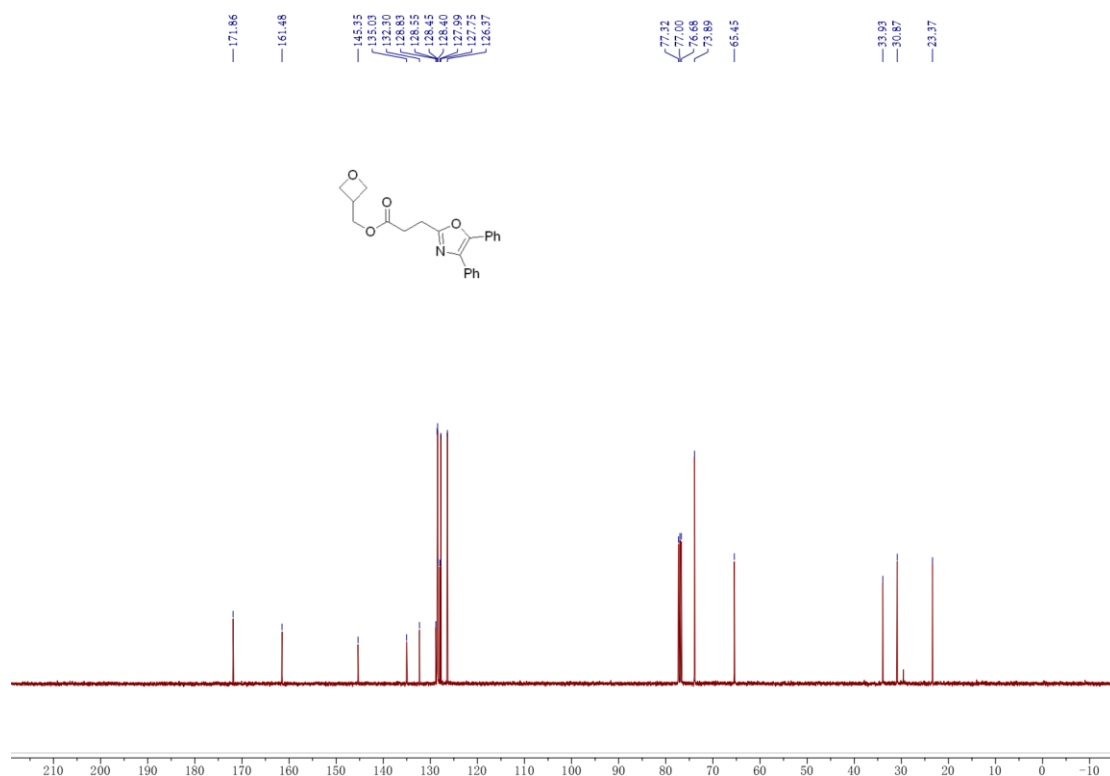
¹³C NMR spectrum of S14



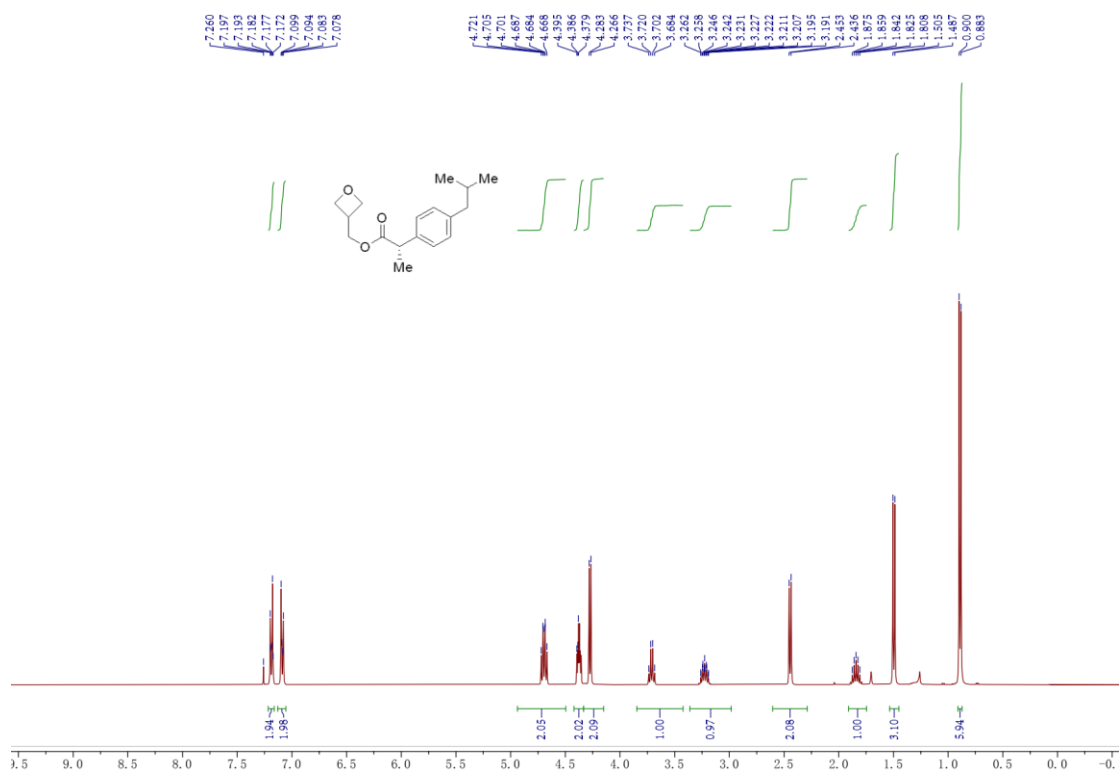
¹H NMR spectrum of S15



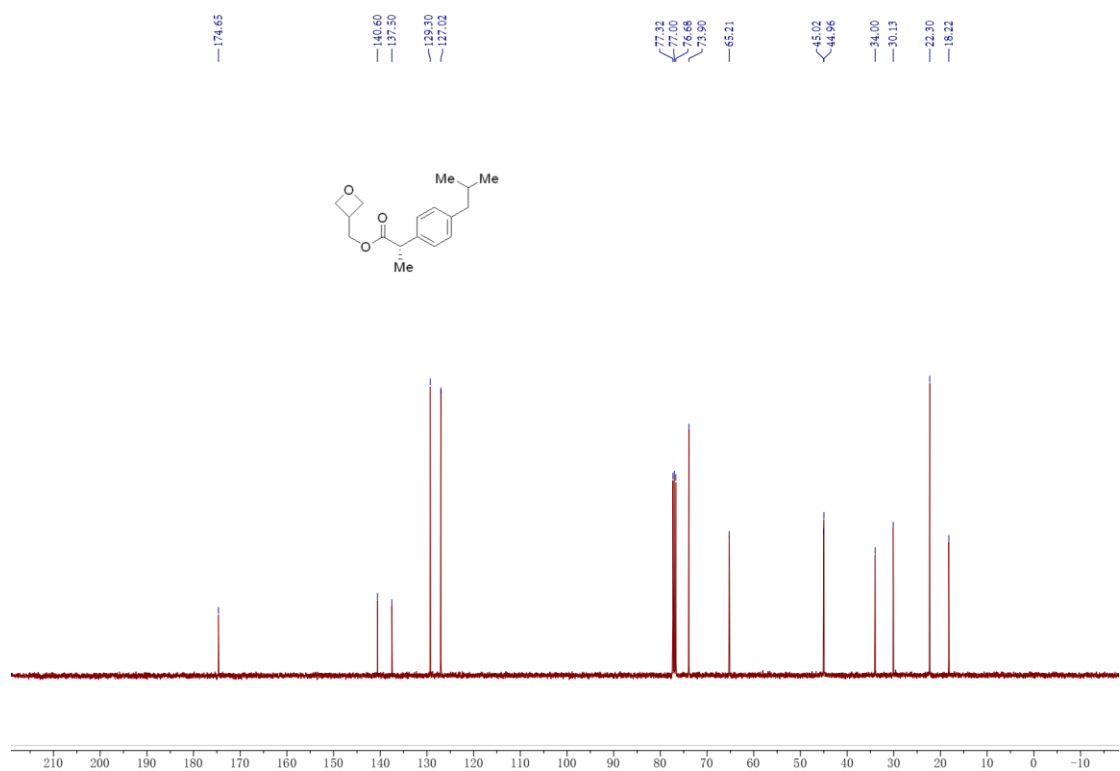
¹³C NMR spectrum of S15



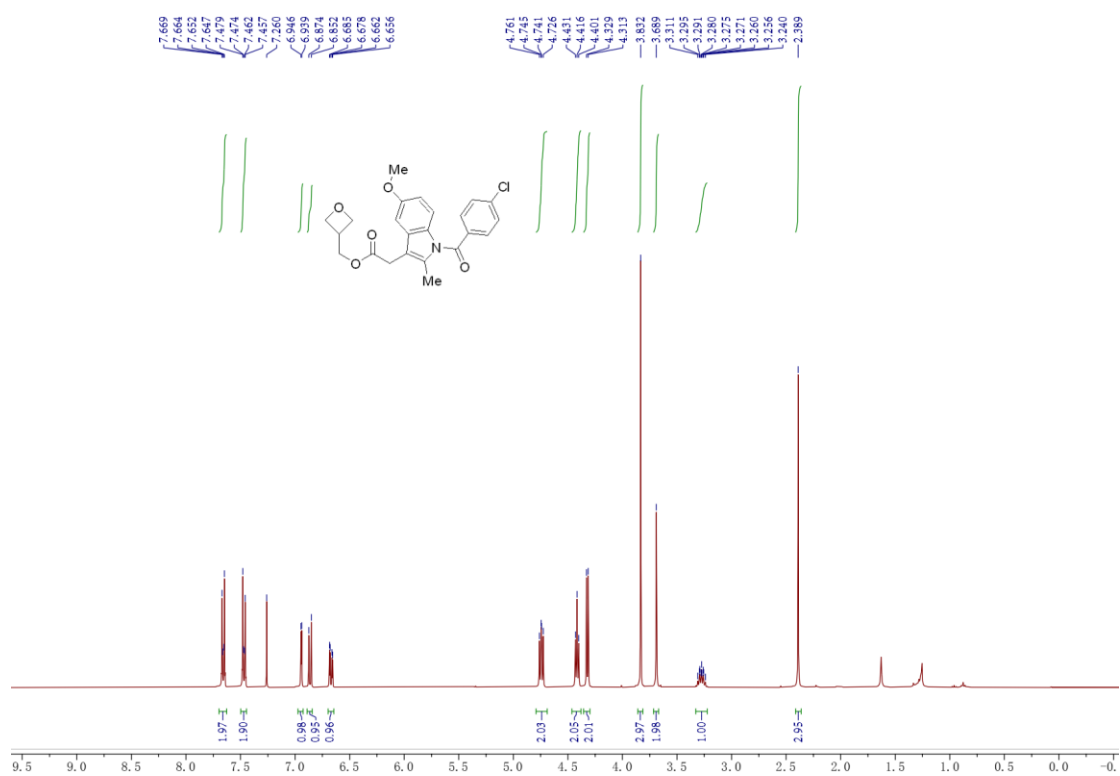
¹H NMR spectrum of S16



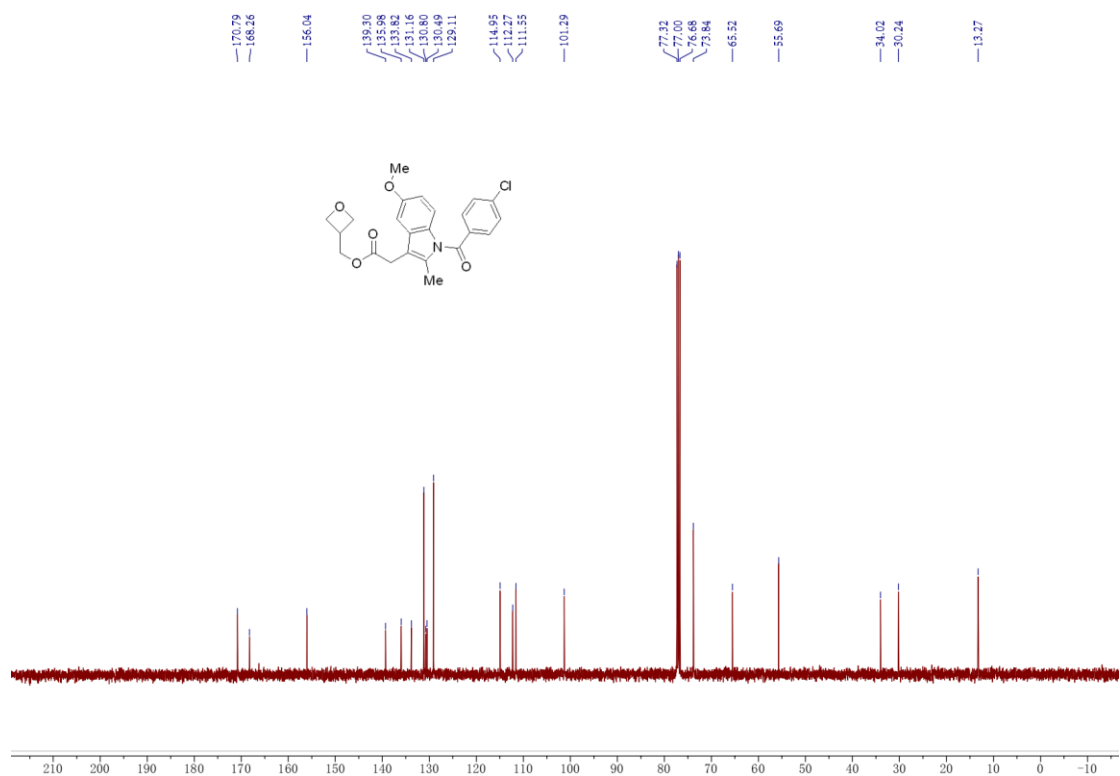
¹³C NMR spectrum of S16



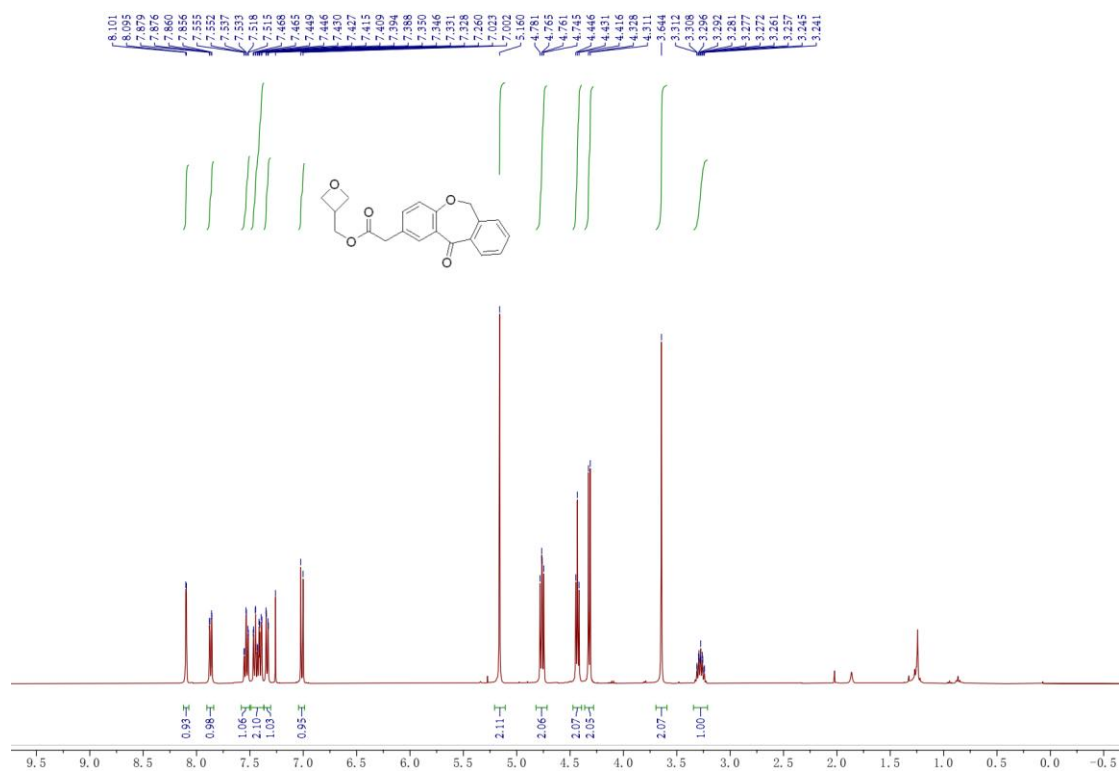
¹H NMR spectrum of S17



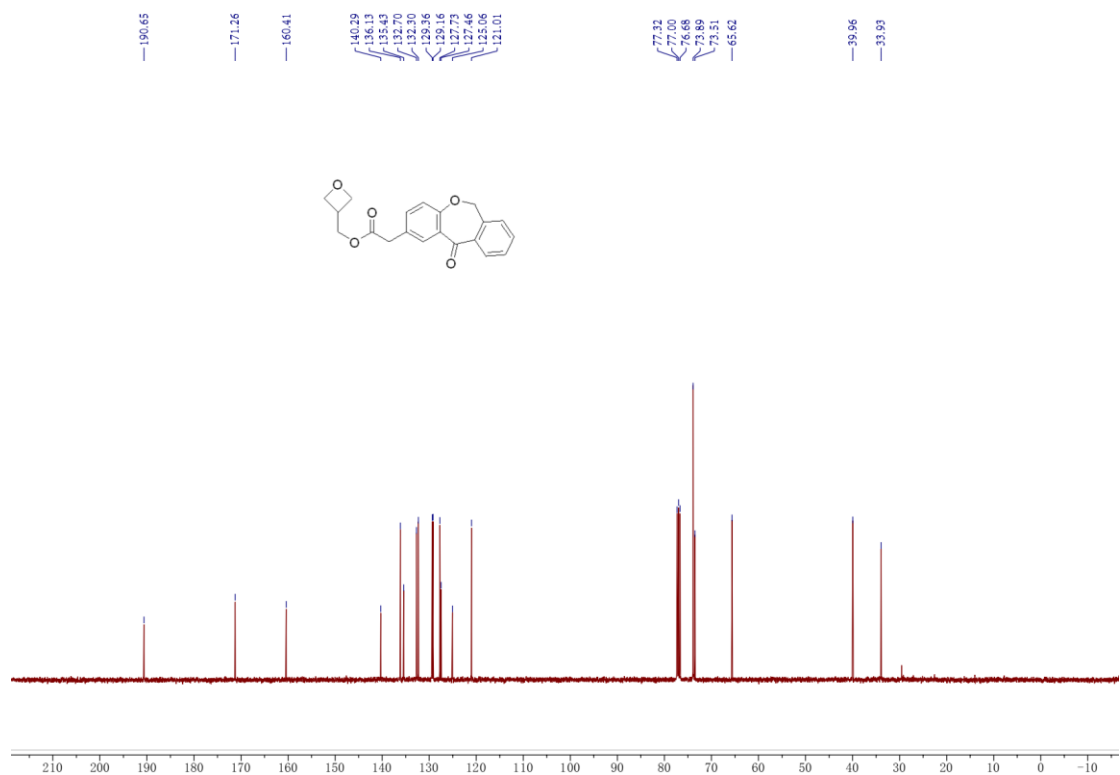
¹³C NMR spectrum of S17



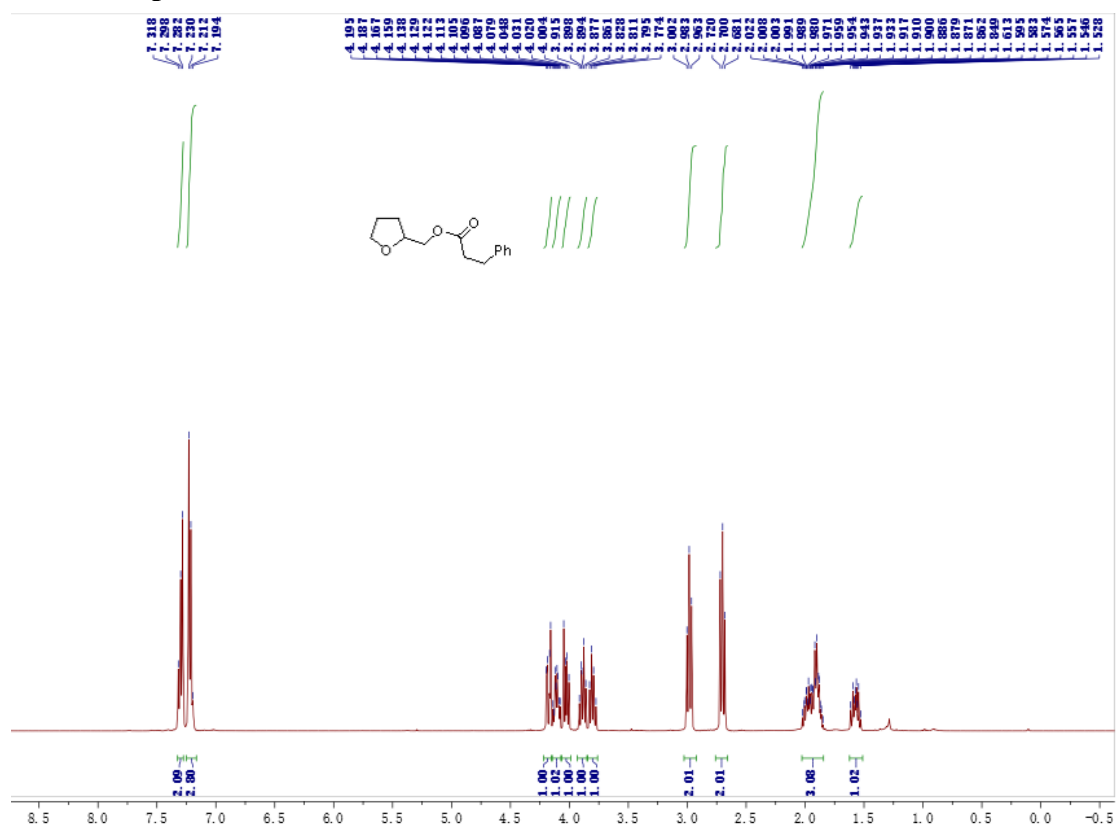
¹H NMR spectrum of S18



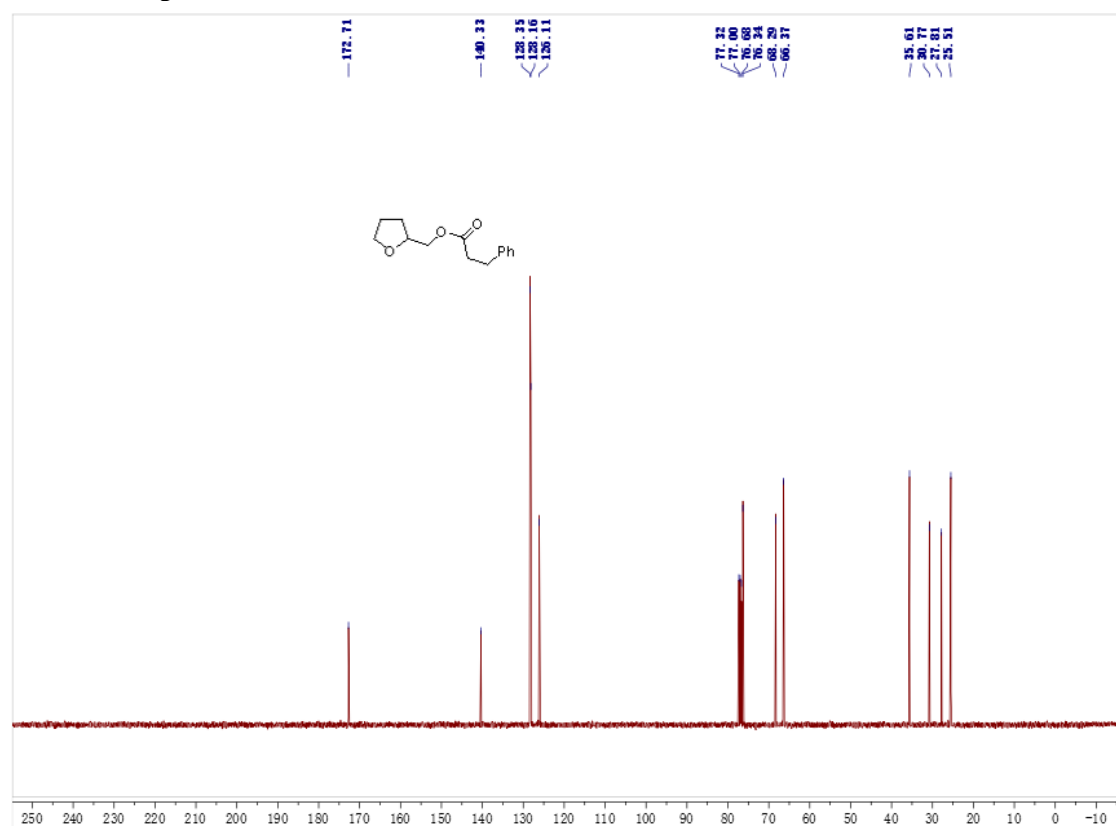
¹³C NMR spectrum of S18



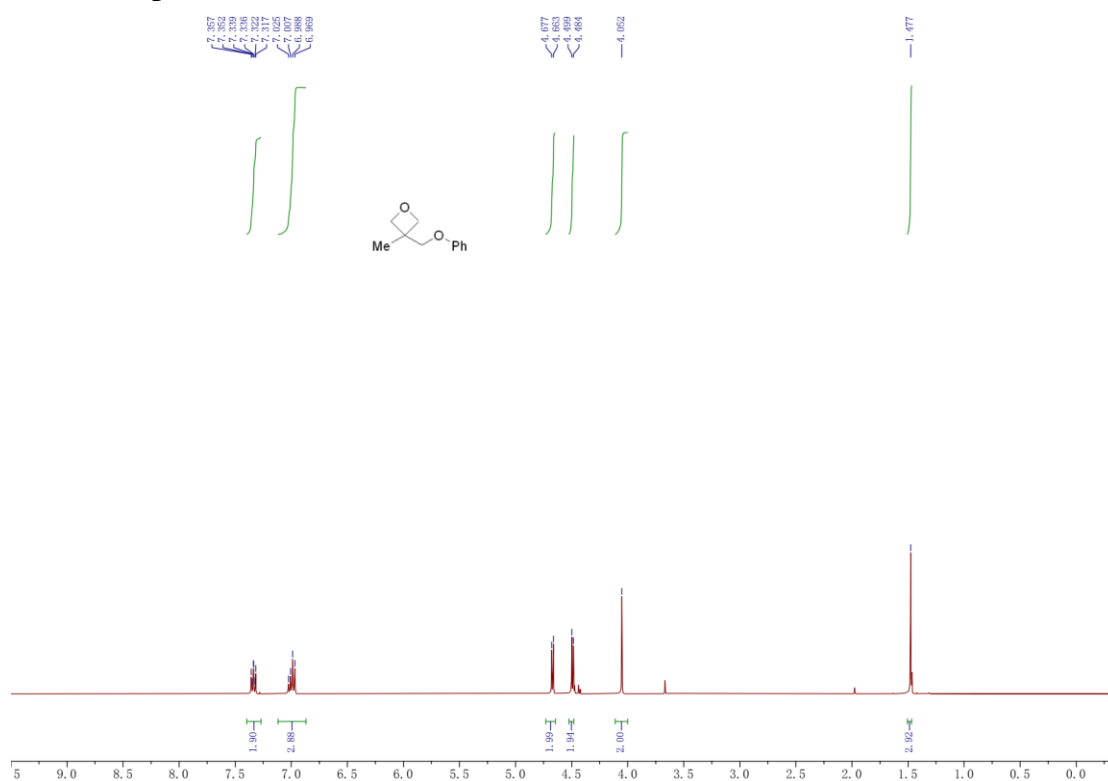
¹H NMR spectrum of S20



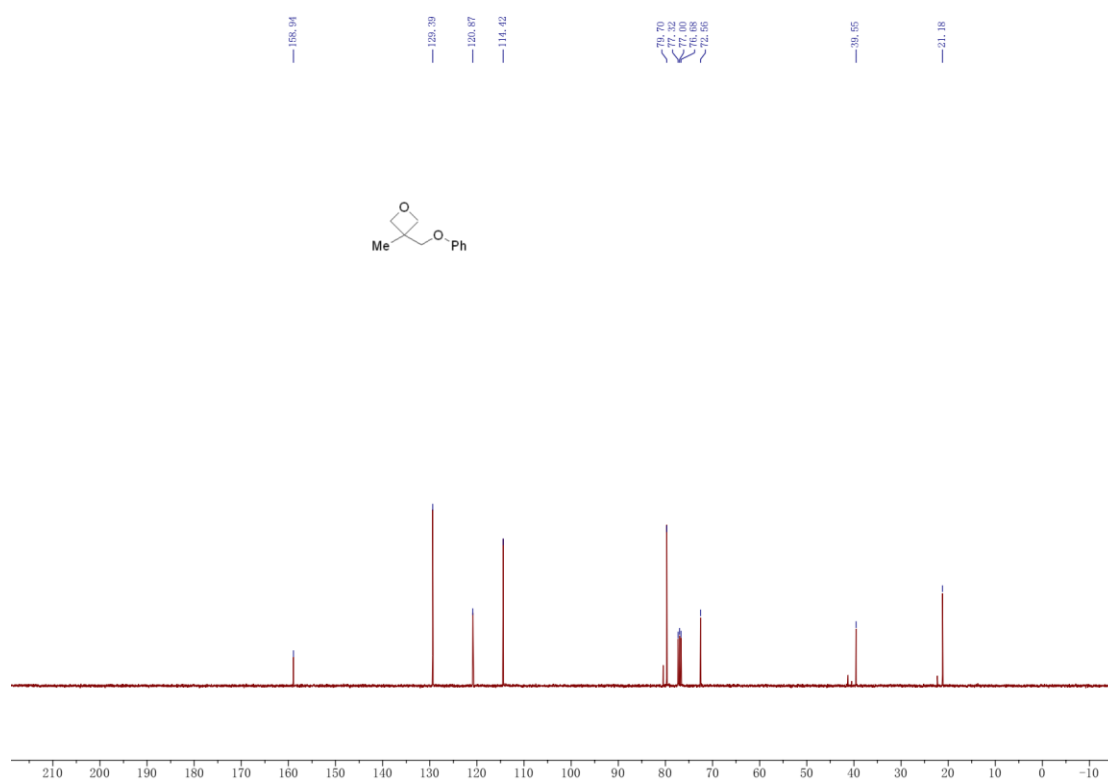
¹³C NMR spectrum of S20



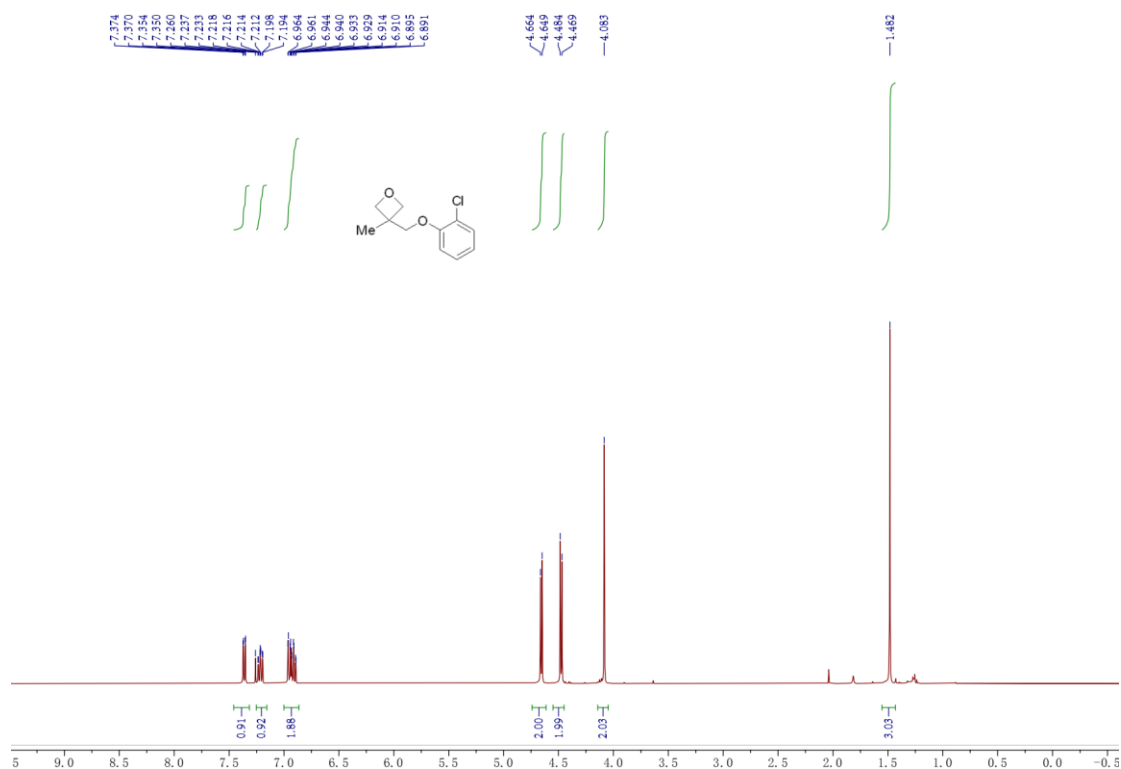
¹H NMR spectrum of S21



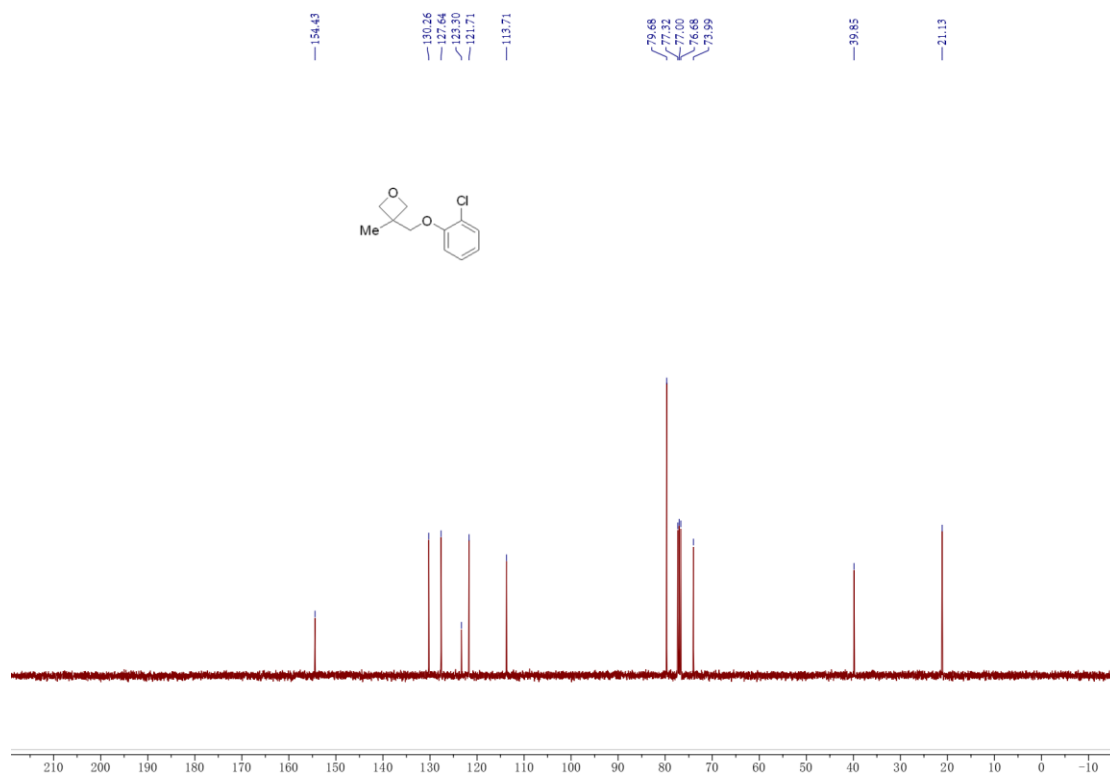
¹³C NMR spectrum of S21



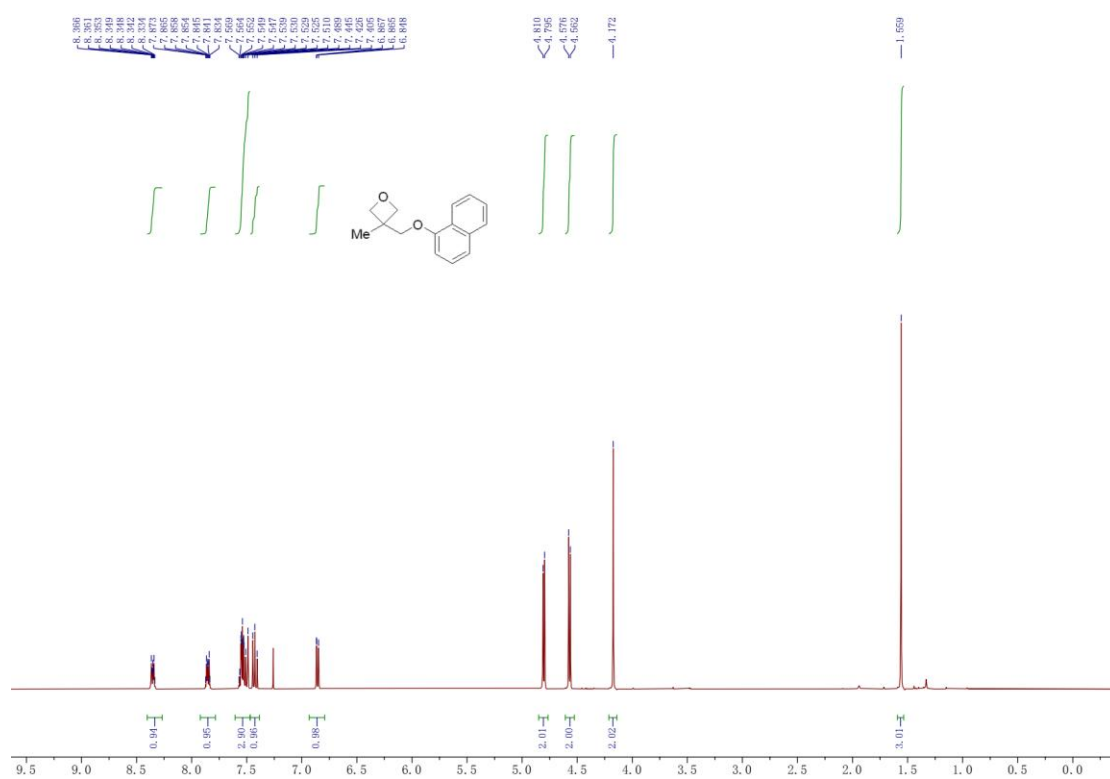
¹H NMR spectrum of S22



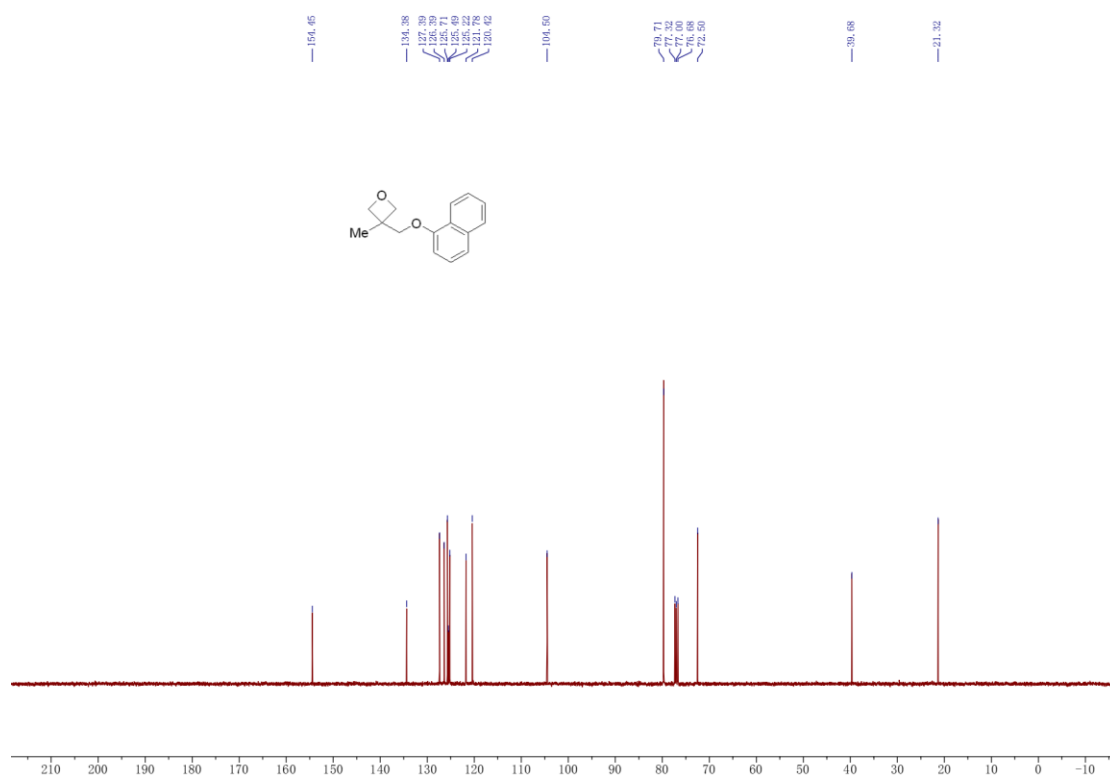
¹³C NMR spectrum of S22



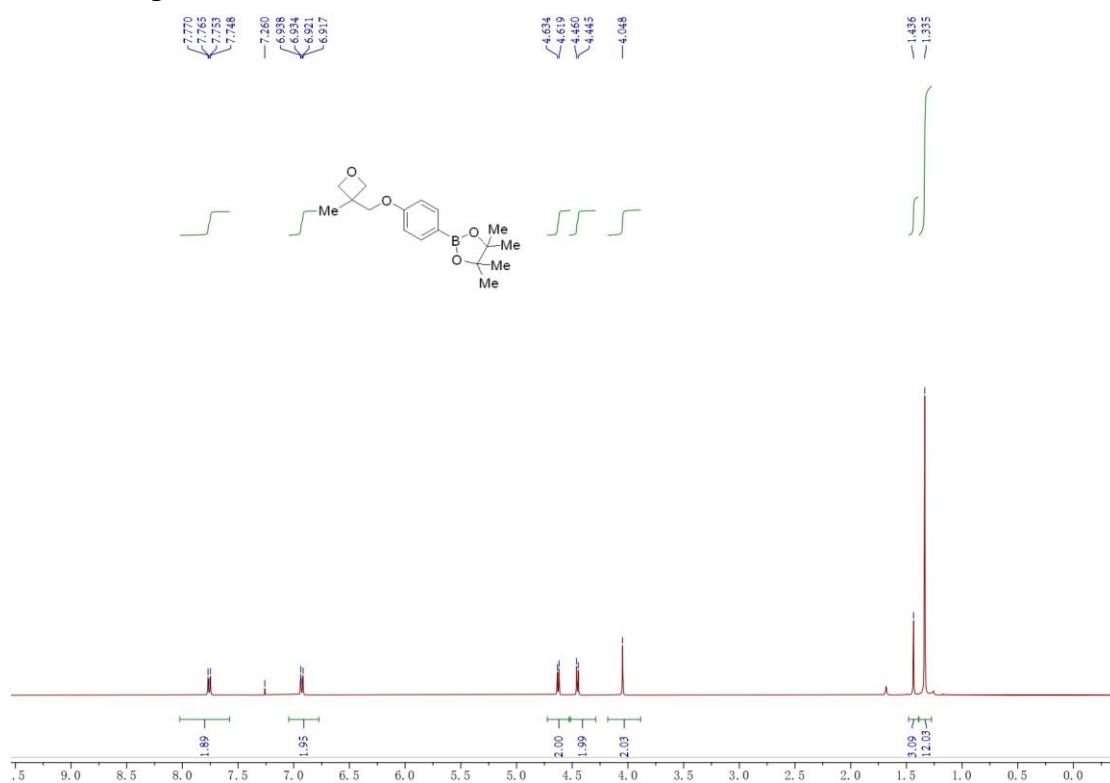
¹H NMR spectrum of S23



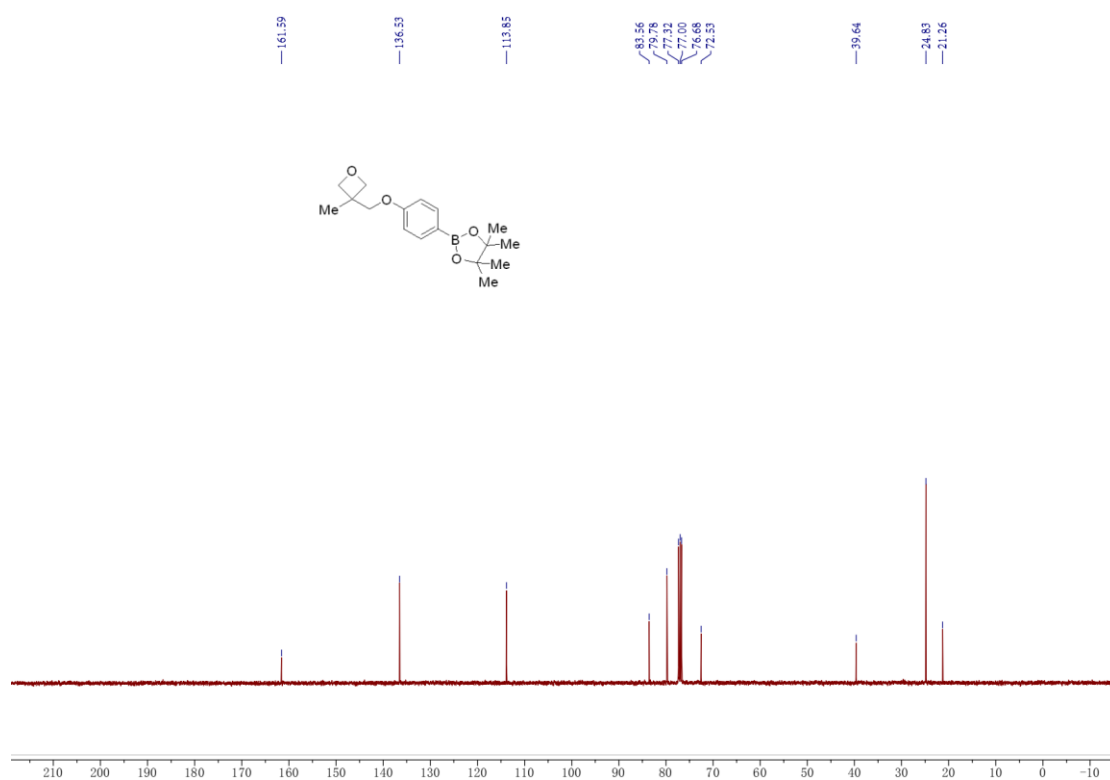
¹³C NMR spectrum of S23



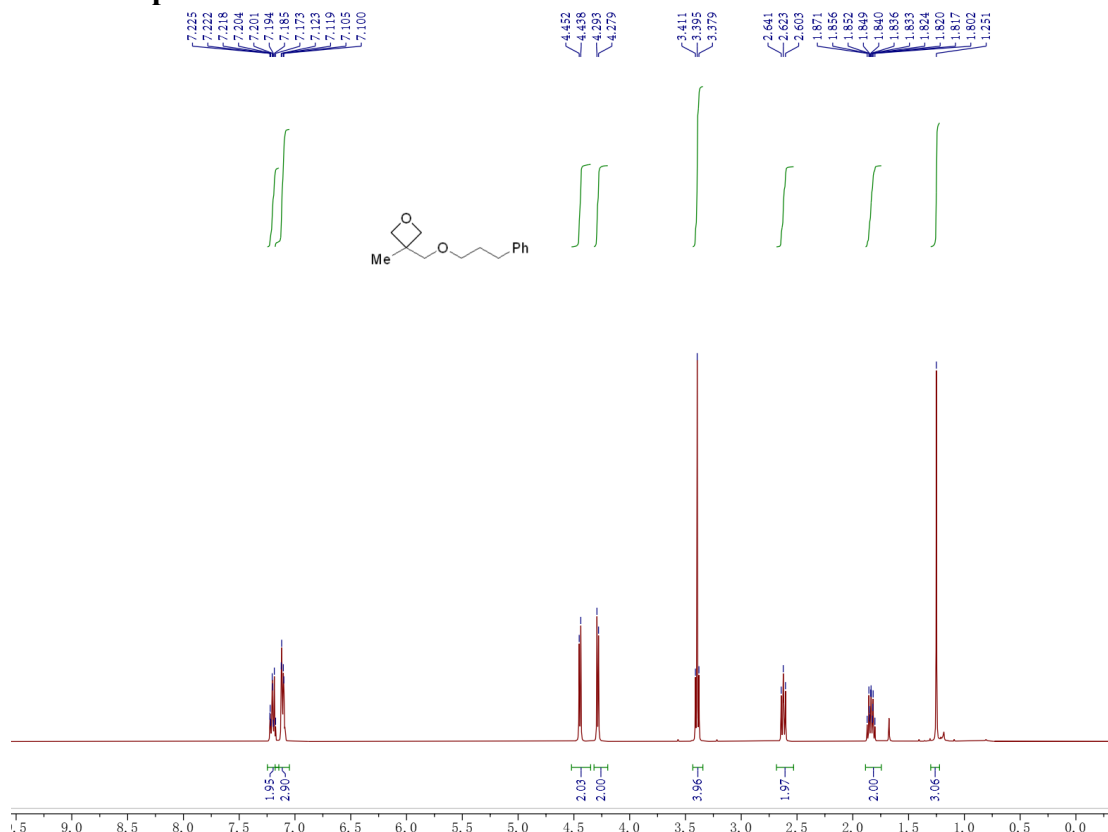
¹H NMR spectrum of S24



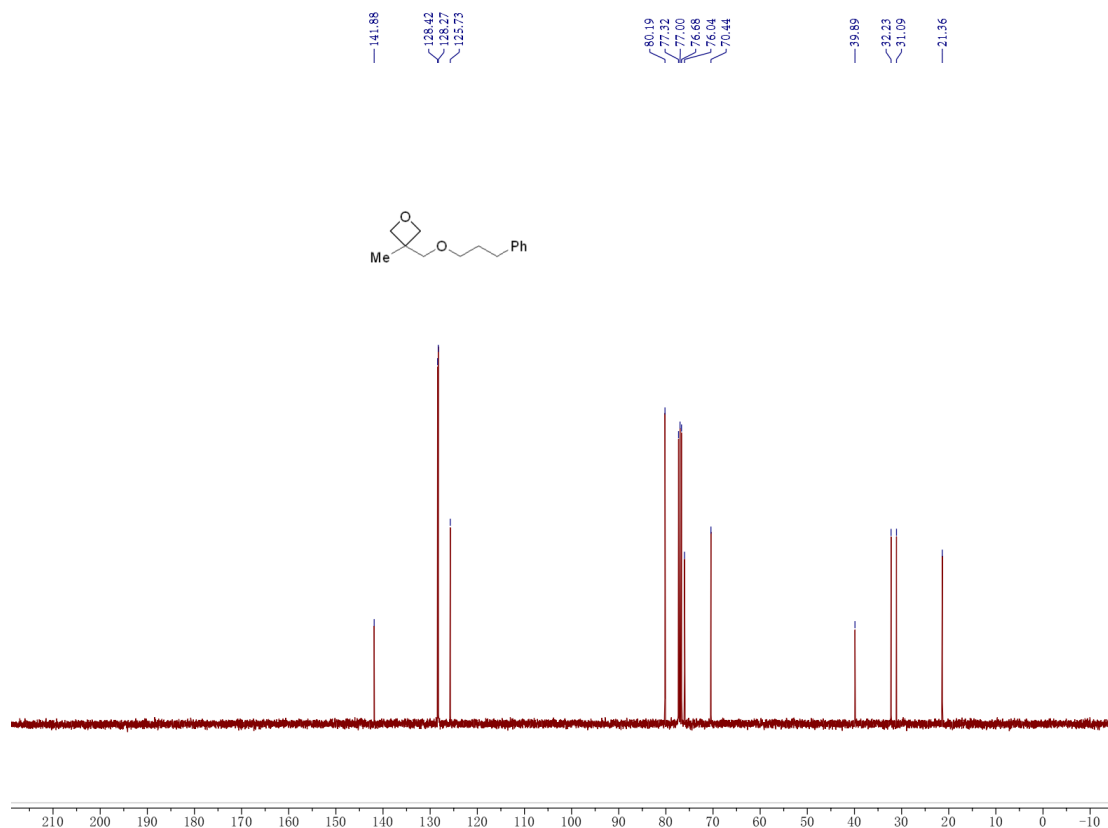
¹³C NMR spectrum of S24



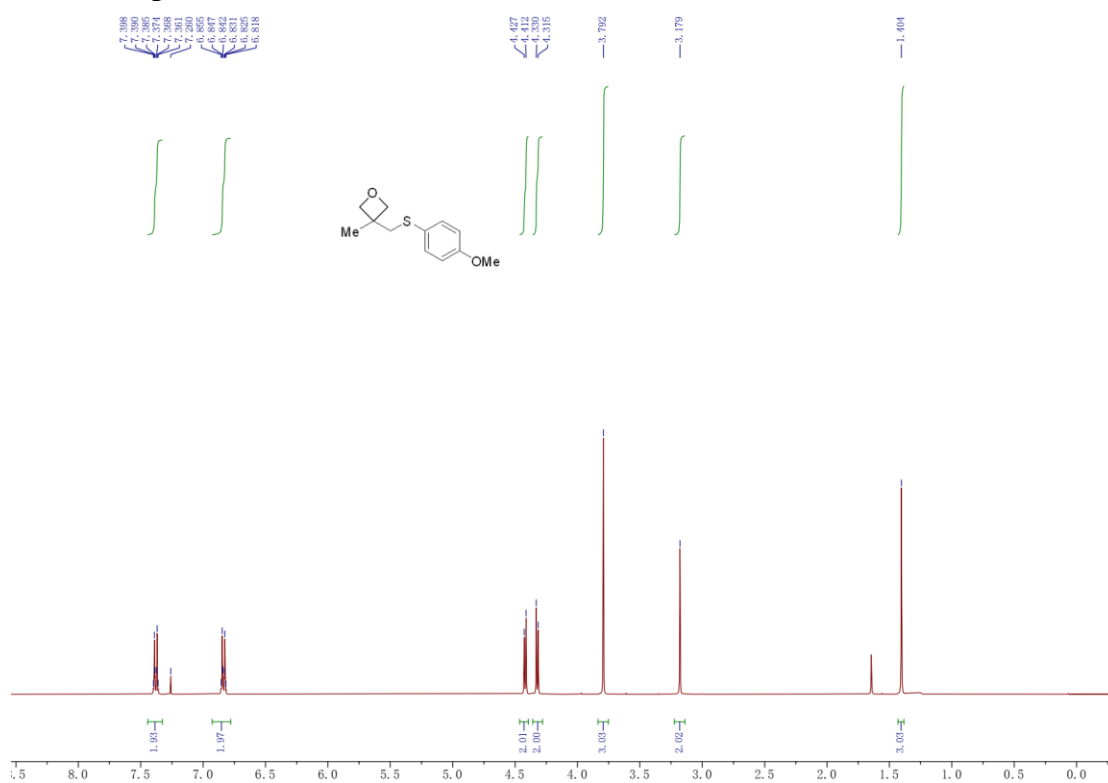
¹H NMR spectrum of S25



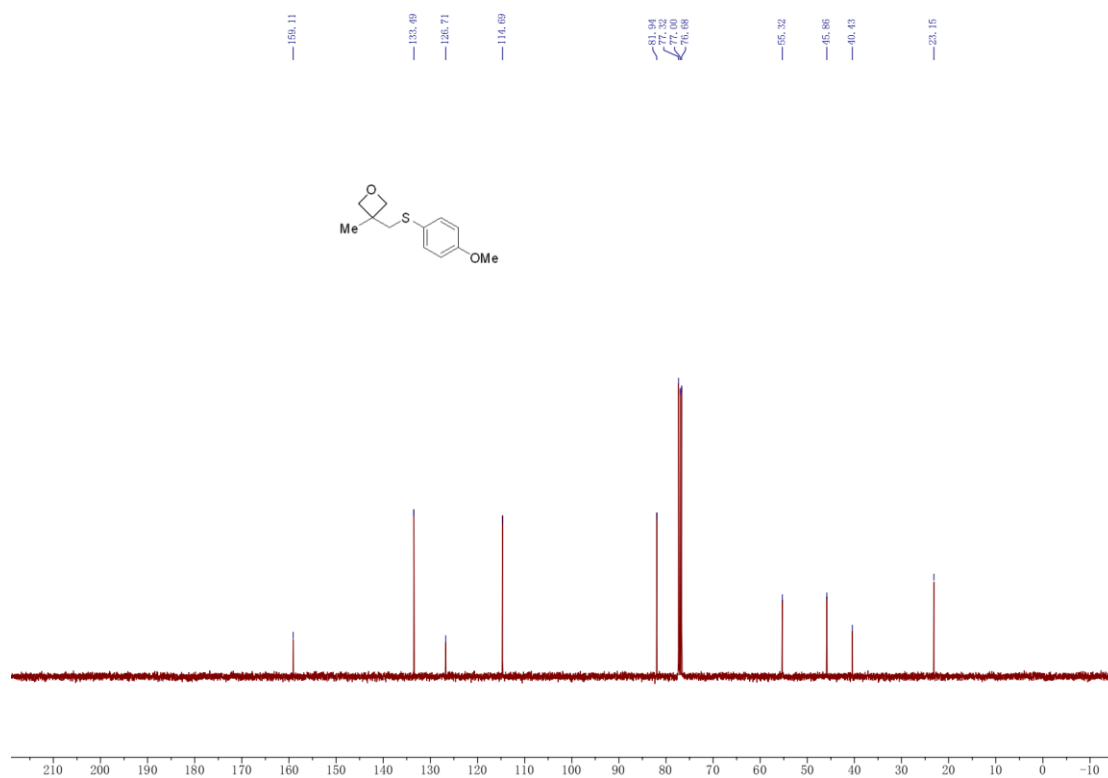
¹³C NMR spectrum of S25



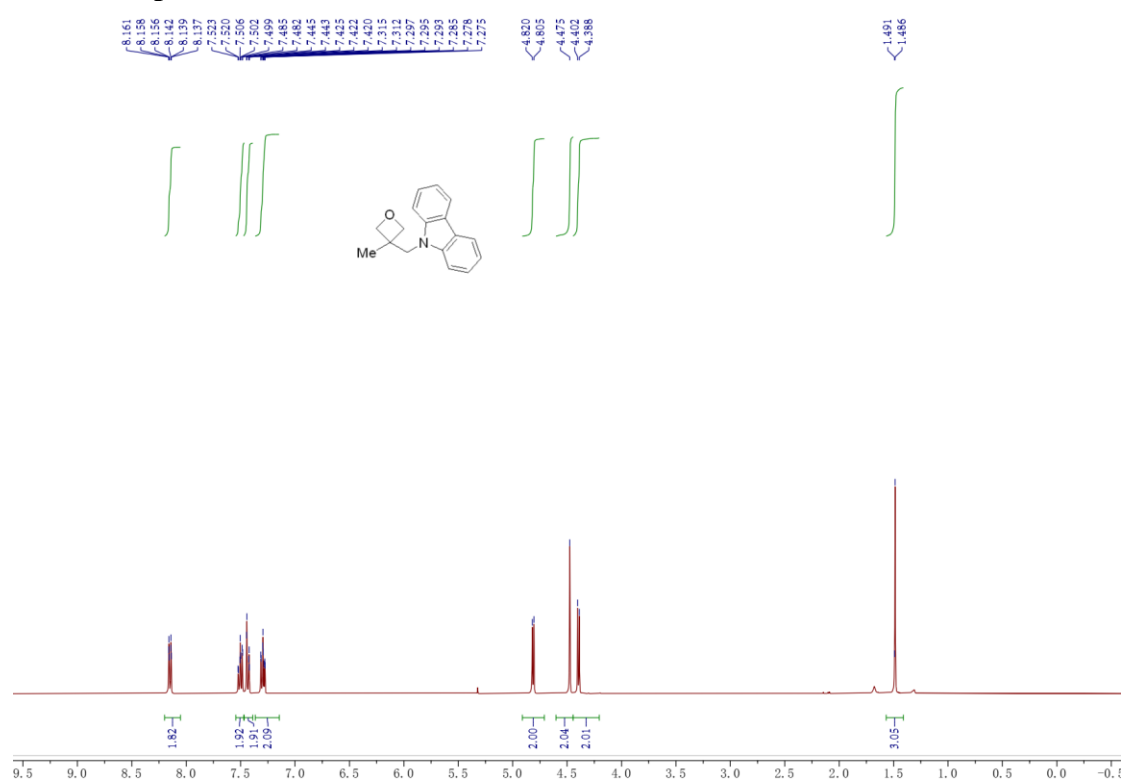
¹H NMR spectrum of S26



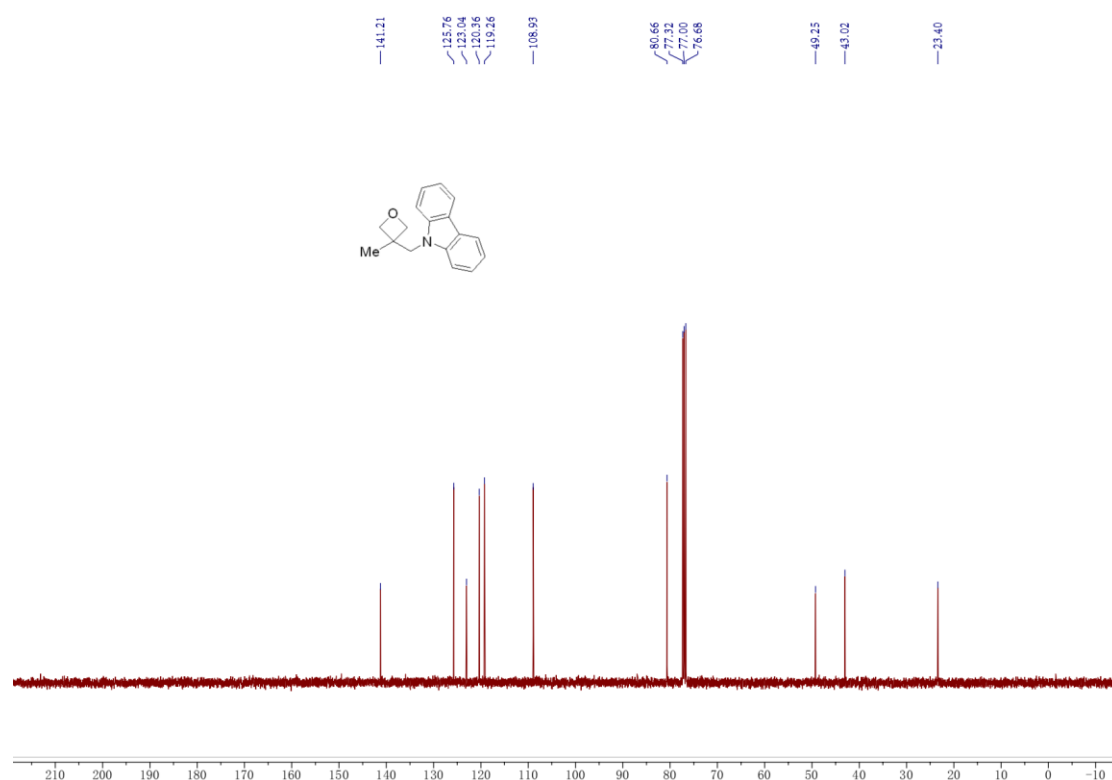
¹³C NMR spectrum of S26



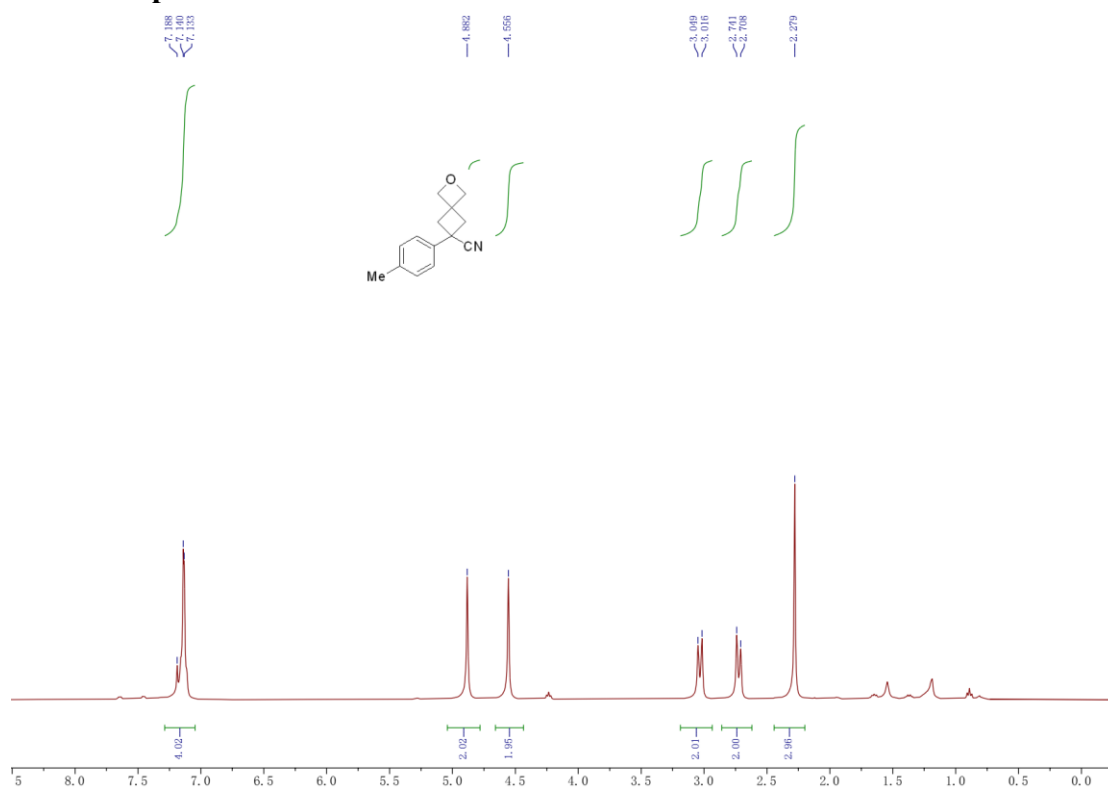
¹H NMR spectrum of S27



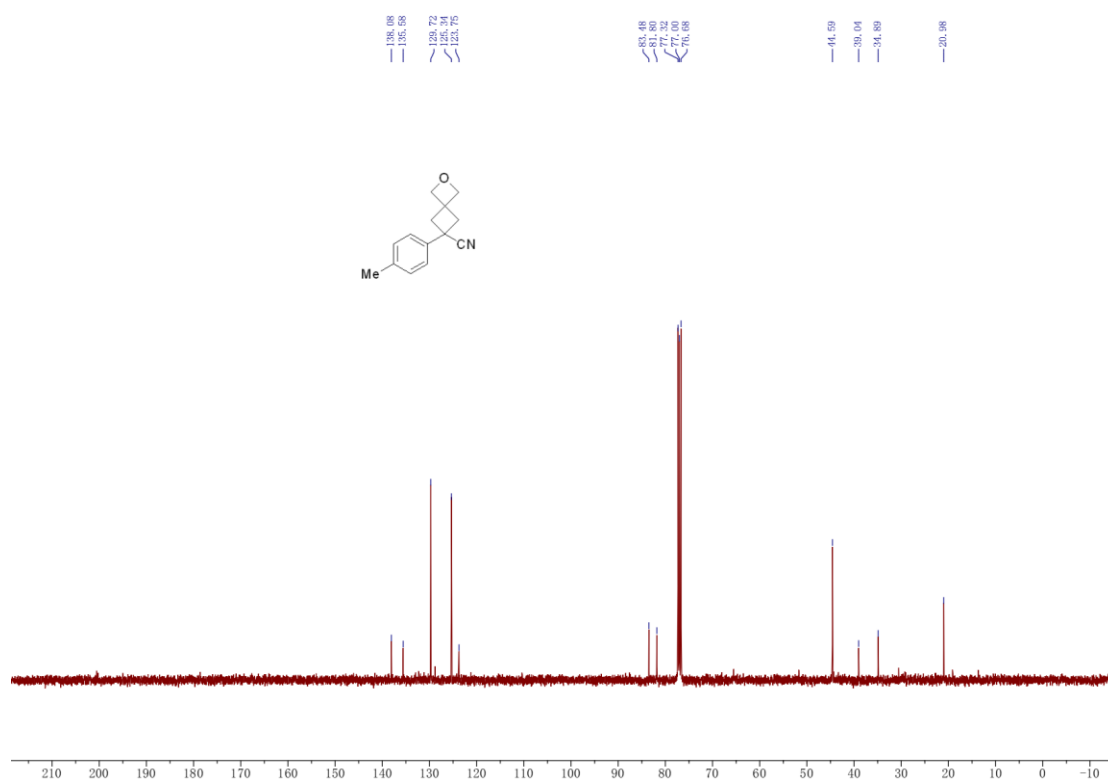
¹³C NMR spectrum of S27



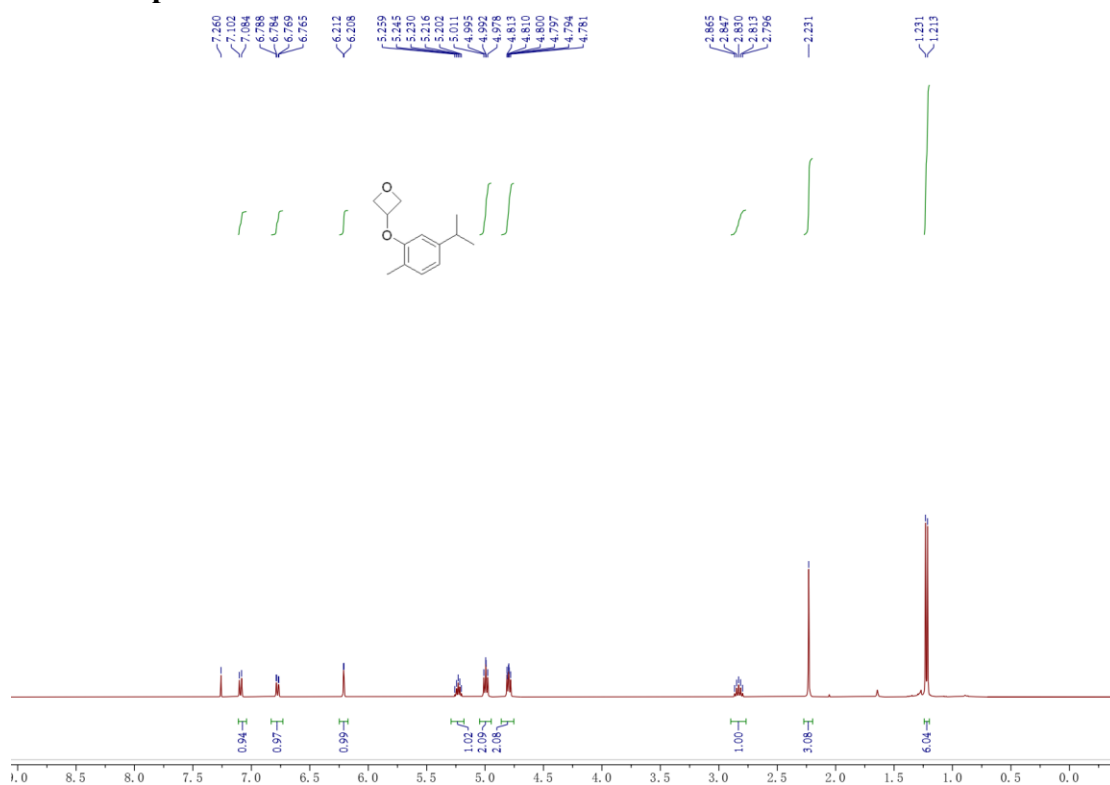
¹H NMR spectrum of S28



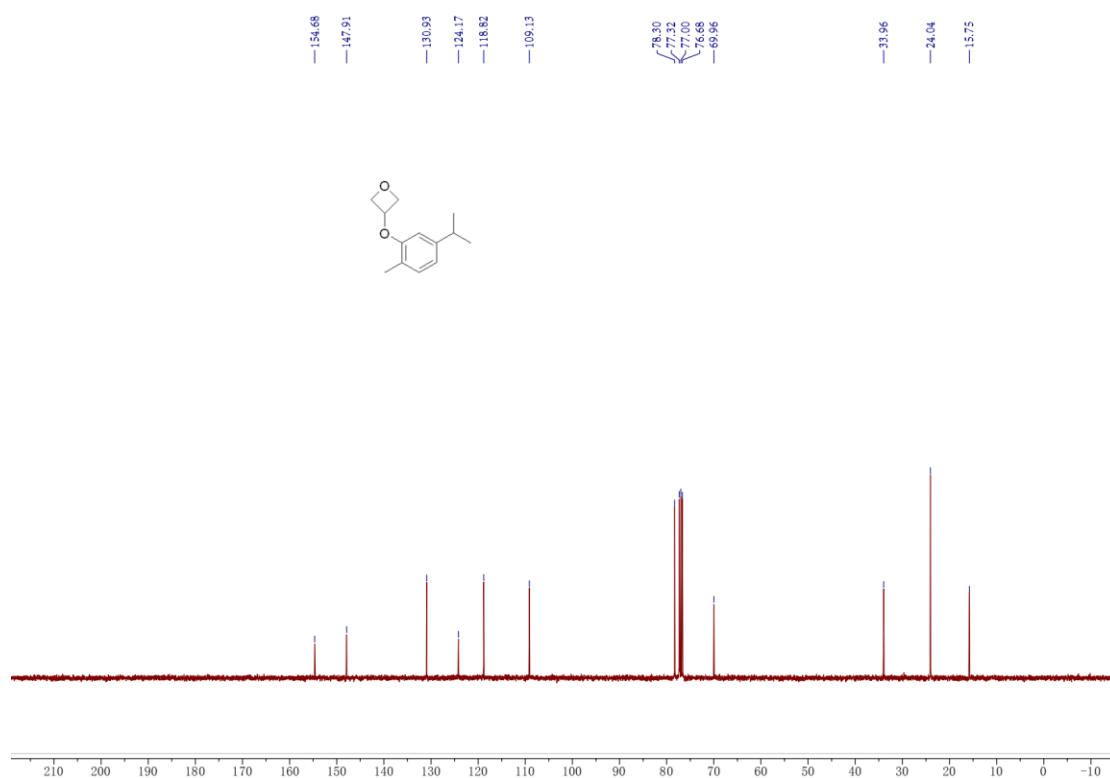
¹³C NMR spectrum of S28



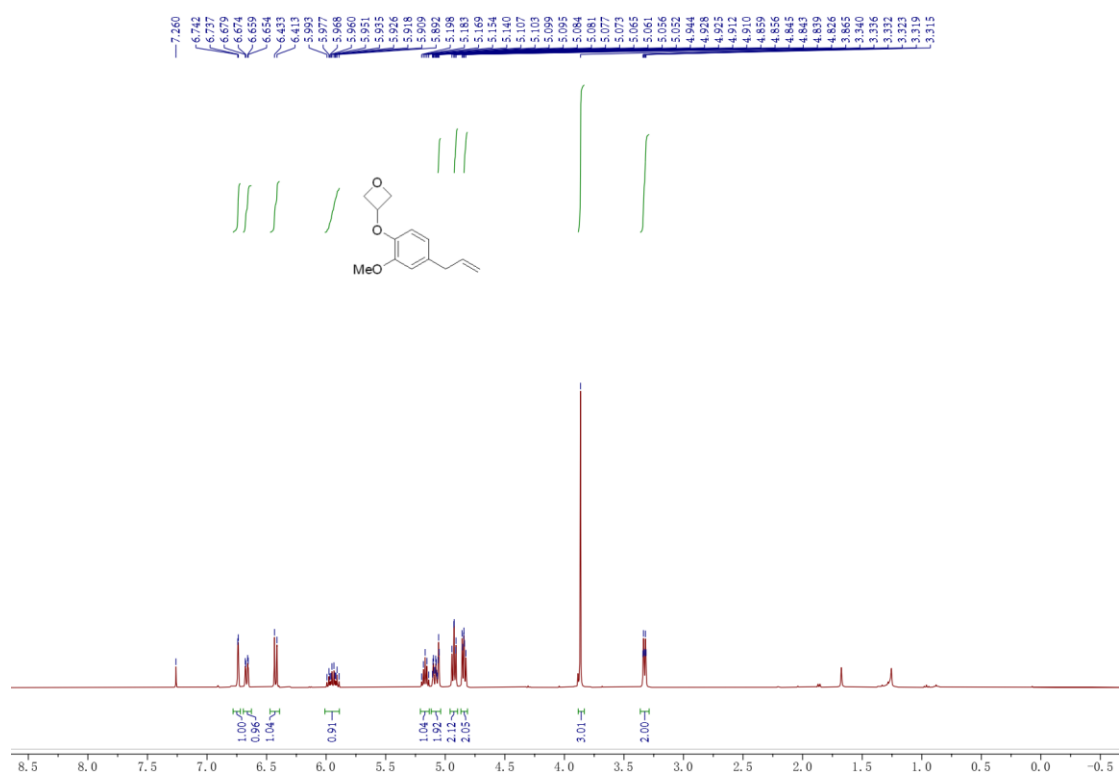
¹H NMR spectrum of S29



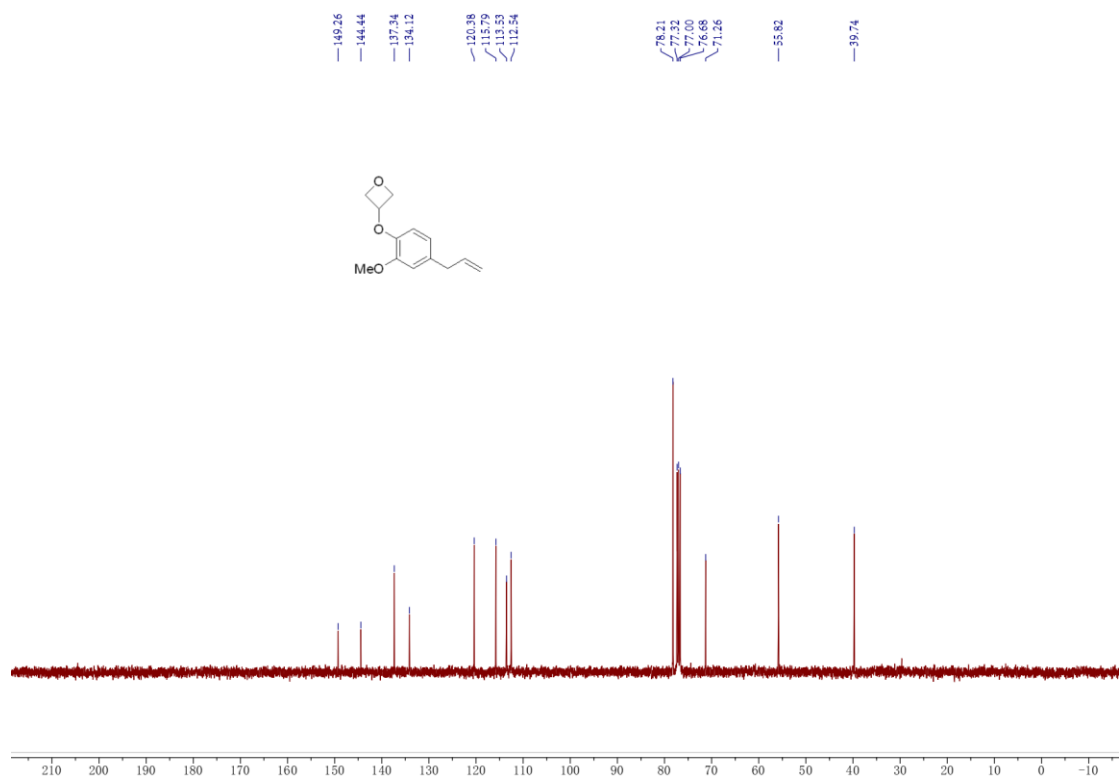
¹³C NMR spectrum of S29



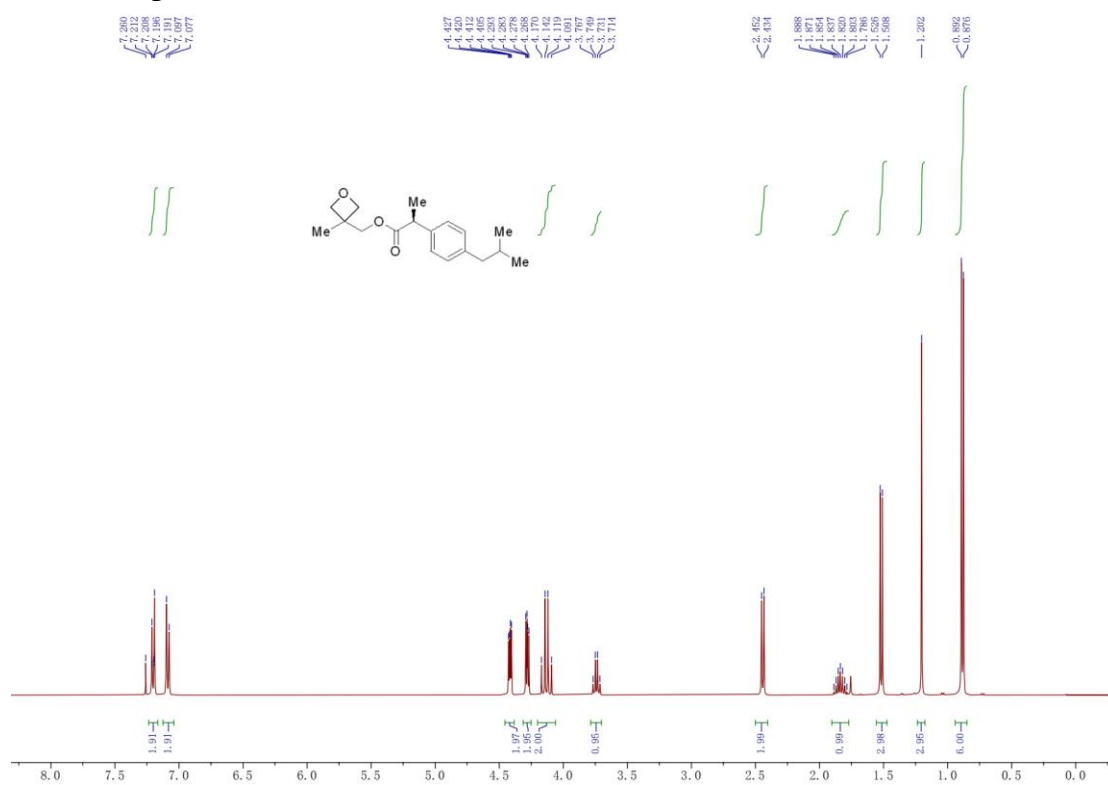
¹H NMR spectrum of S30



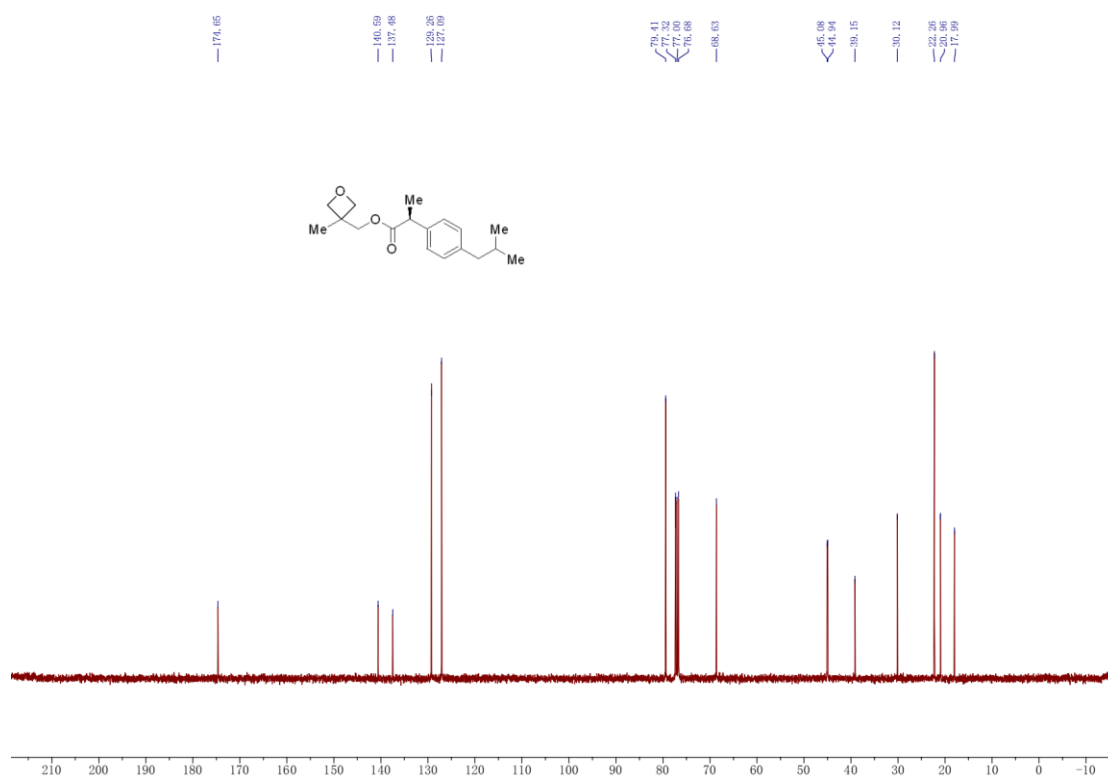
¹³C NMR spectrum of S30



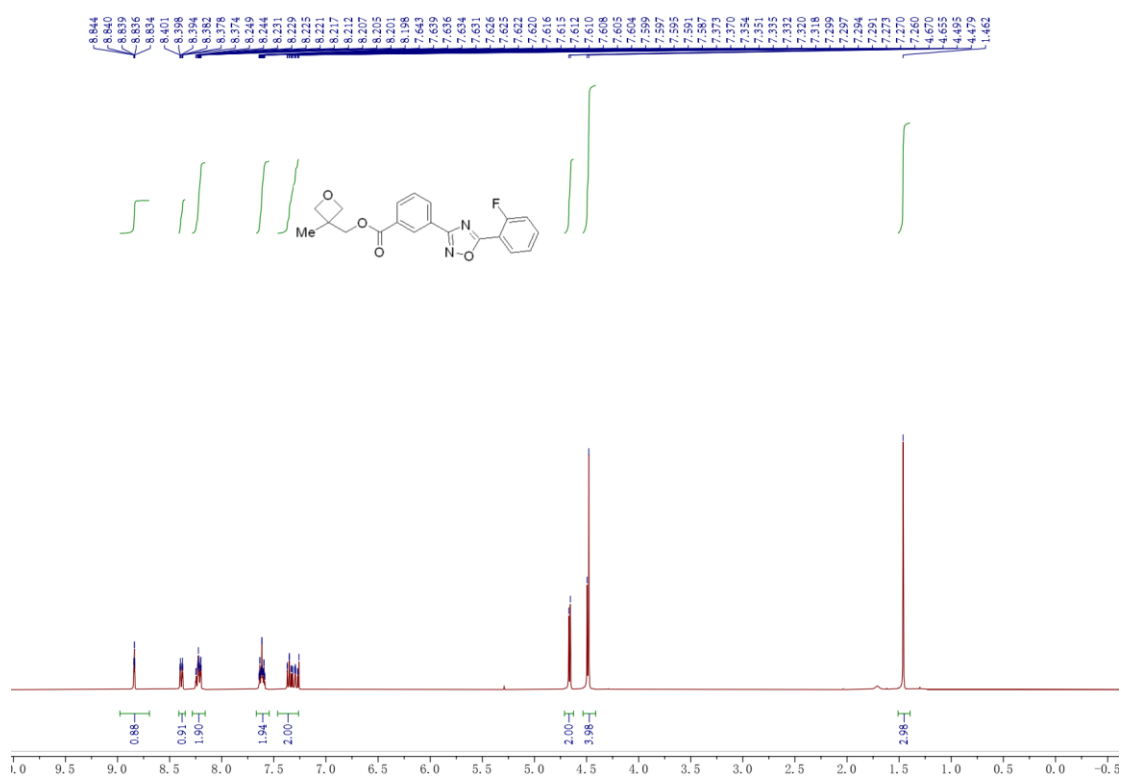
¹H NMR spectrum of S31



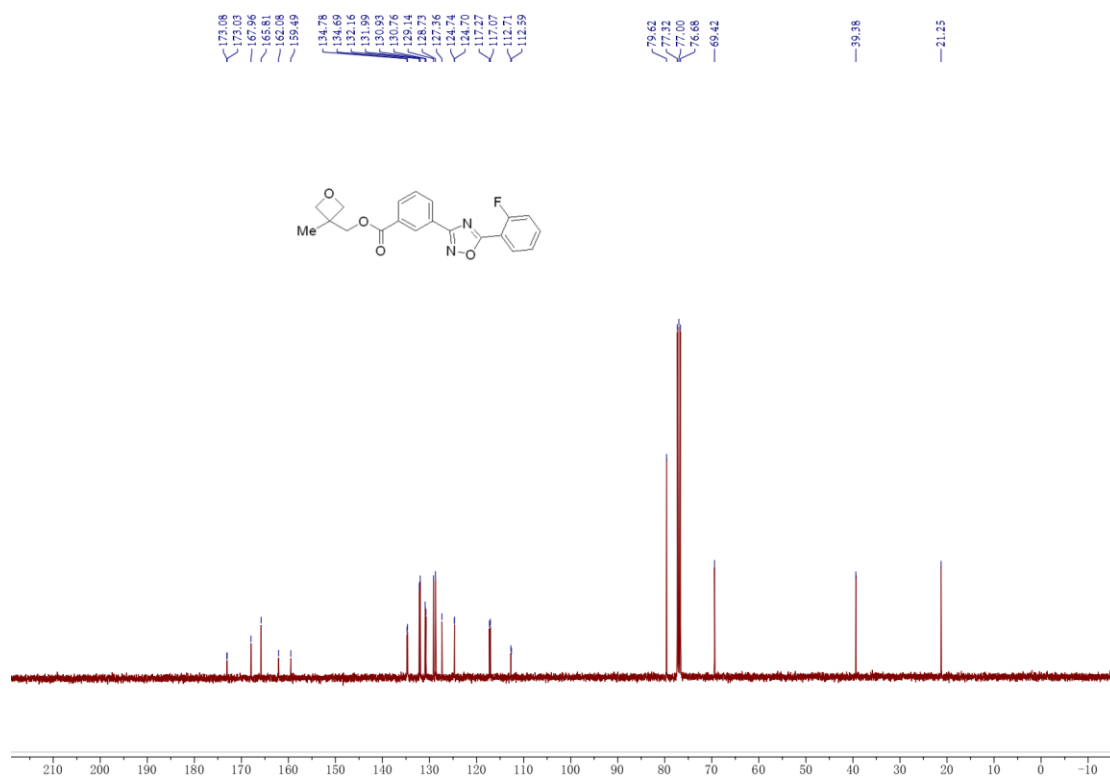
¹³C NMR spectrum of S31



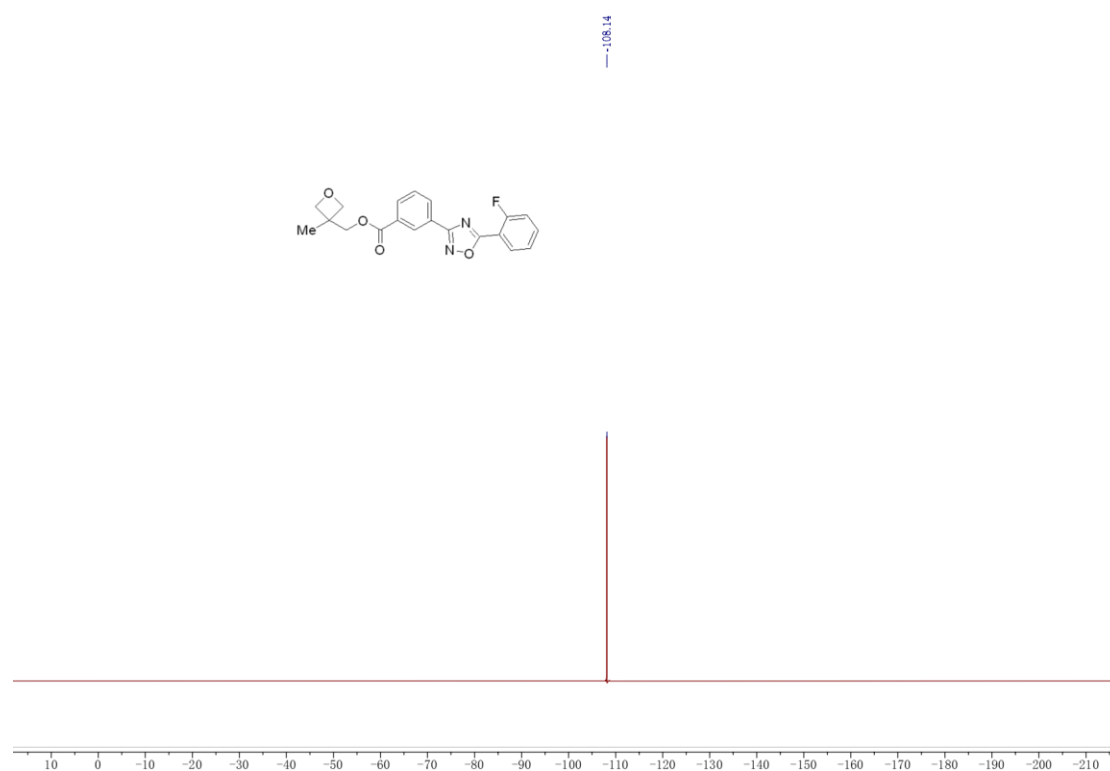
¹H NMR spectrum of S32



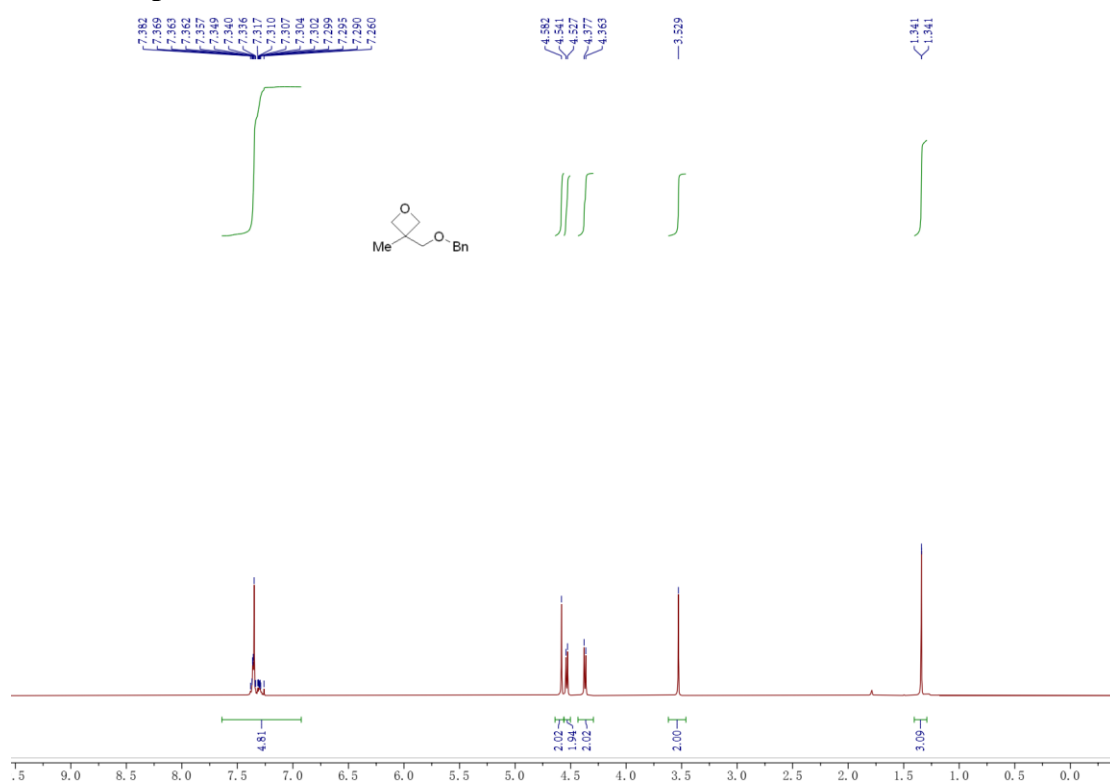
¹³C NMR spectrum of S32



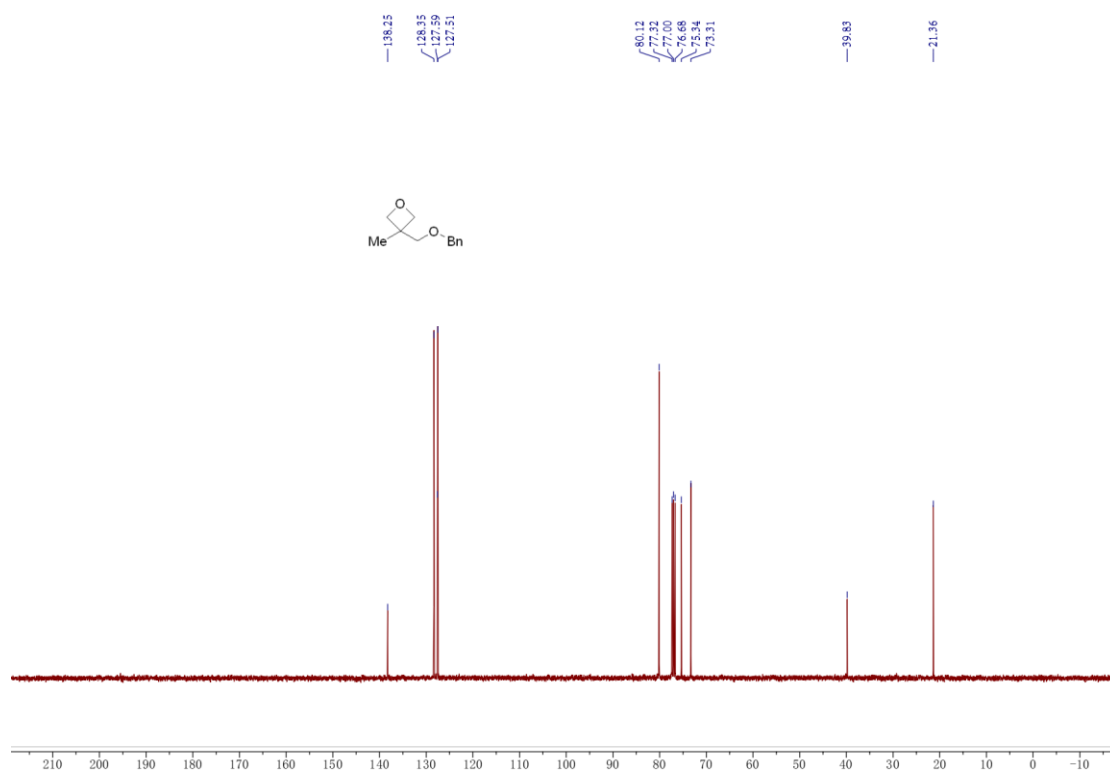
¹⁹F NMR spectrum of S32



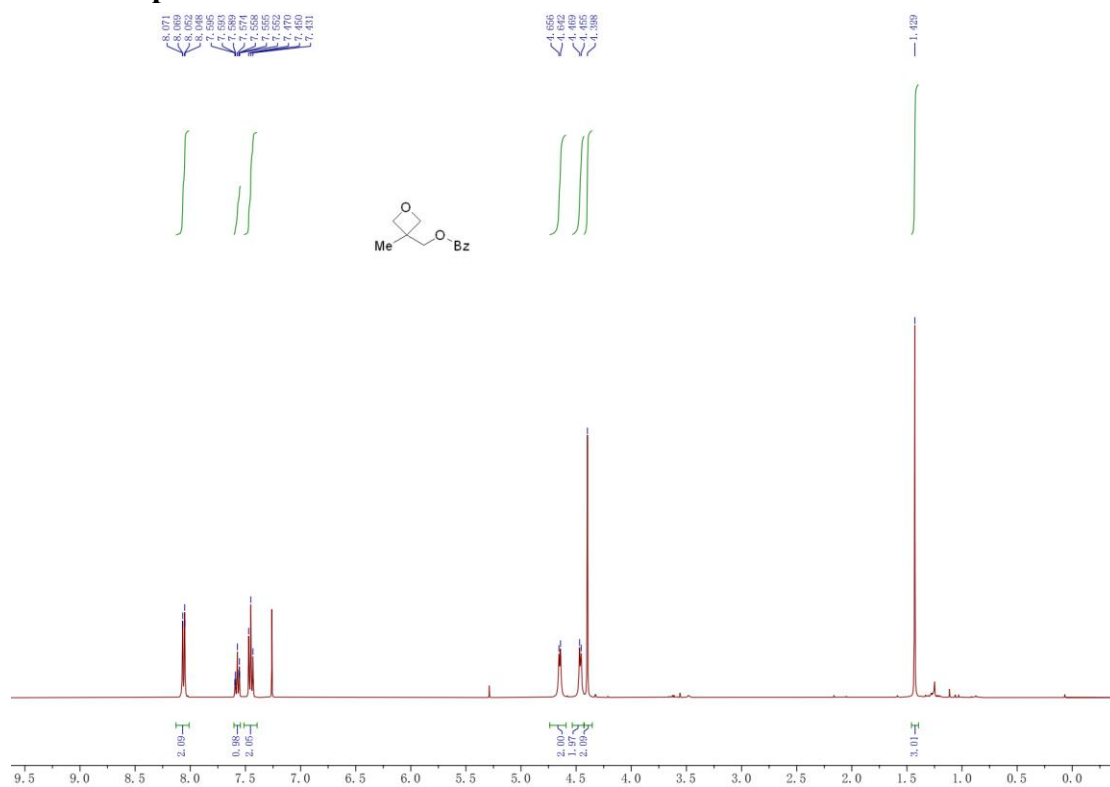
¹H NMR spectrum of S33



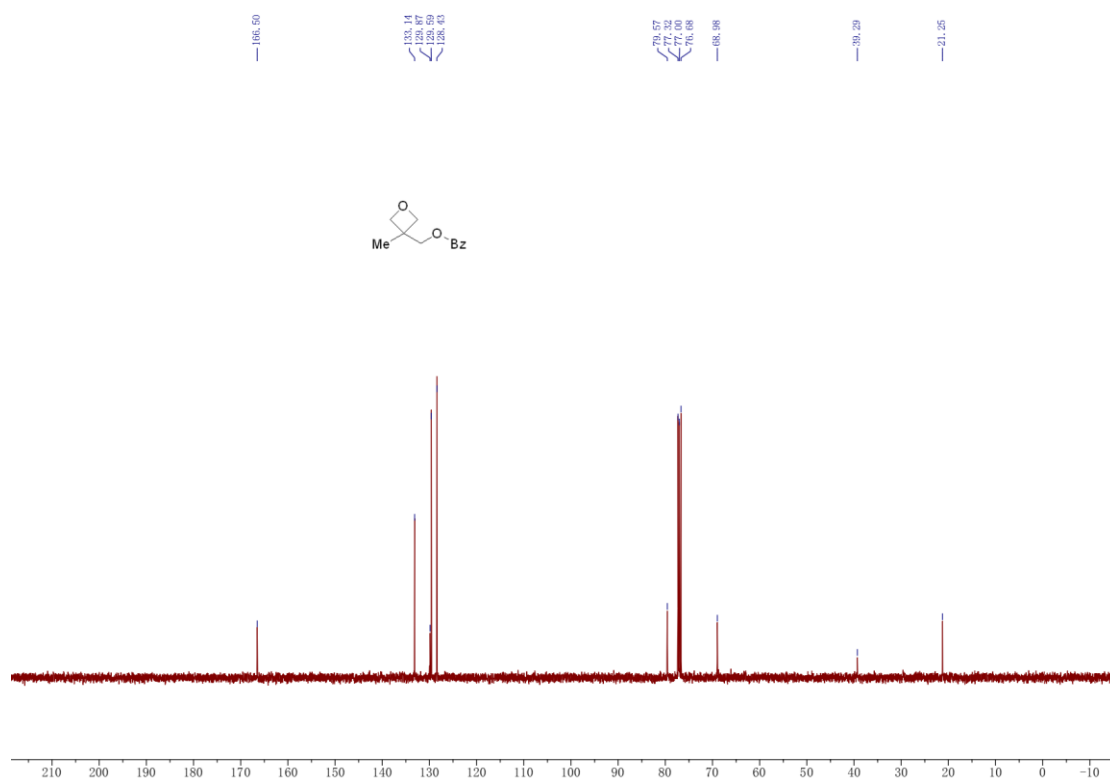
¹³C NMR spectrum of S33



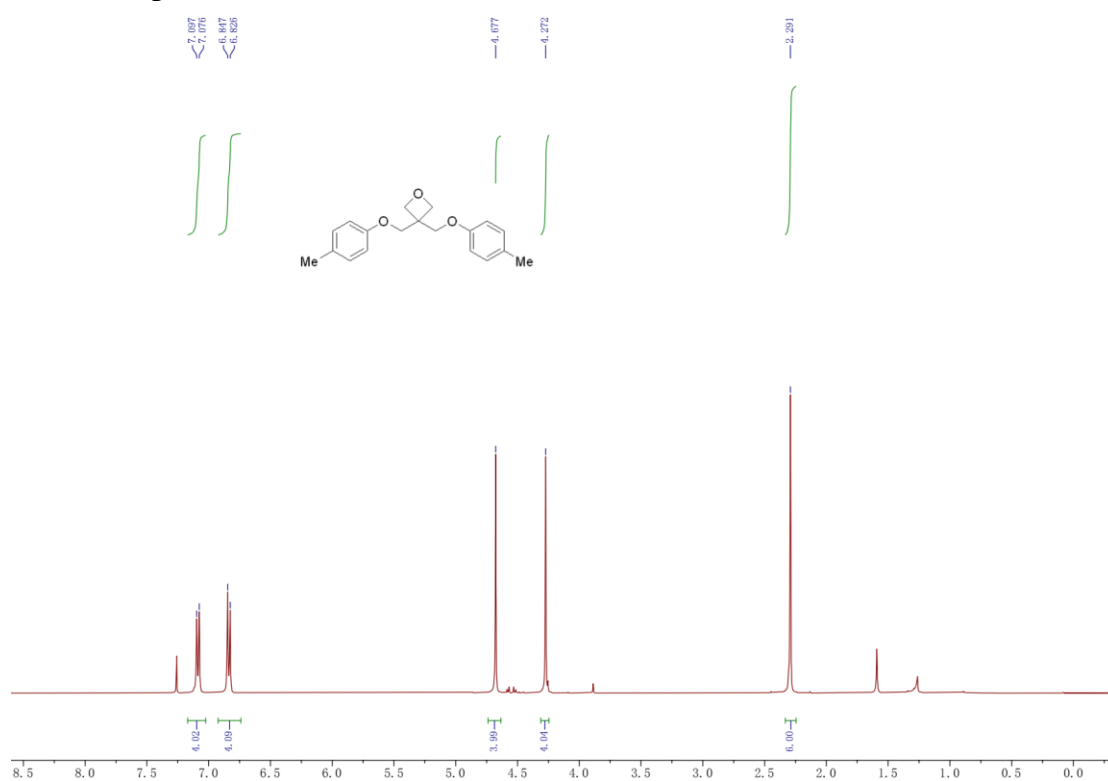
¹H NMR spectrum of S34



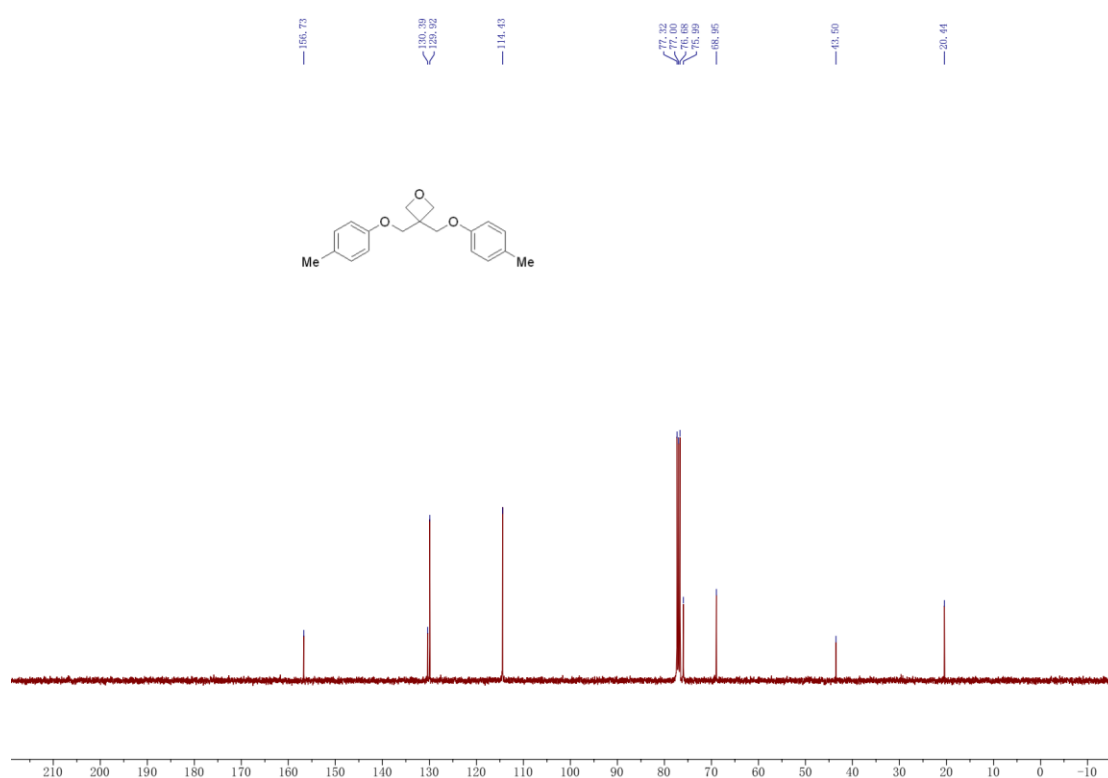
¹³C NMR spectrum of S34



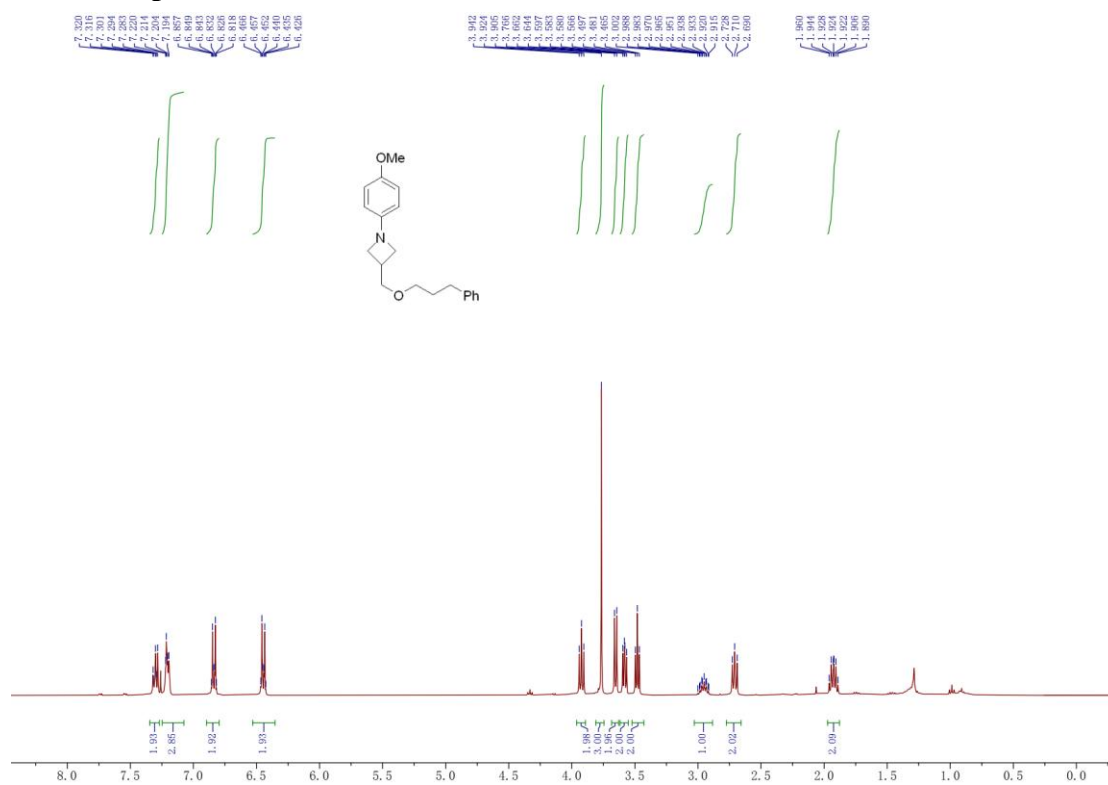
¹H NMR spectrum of S35



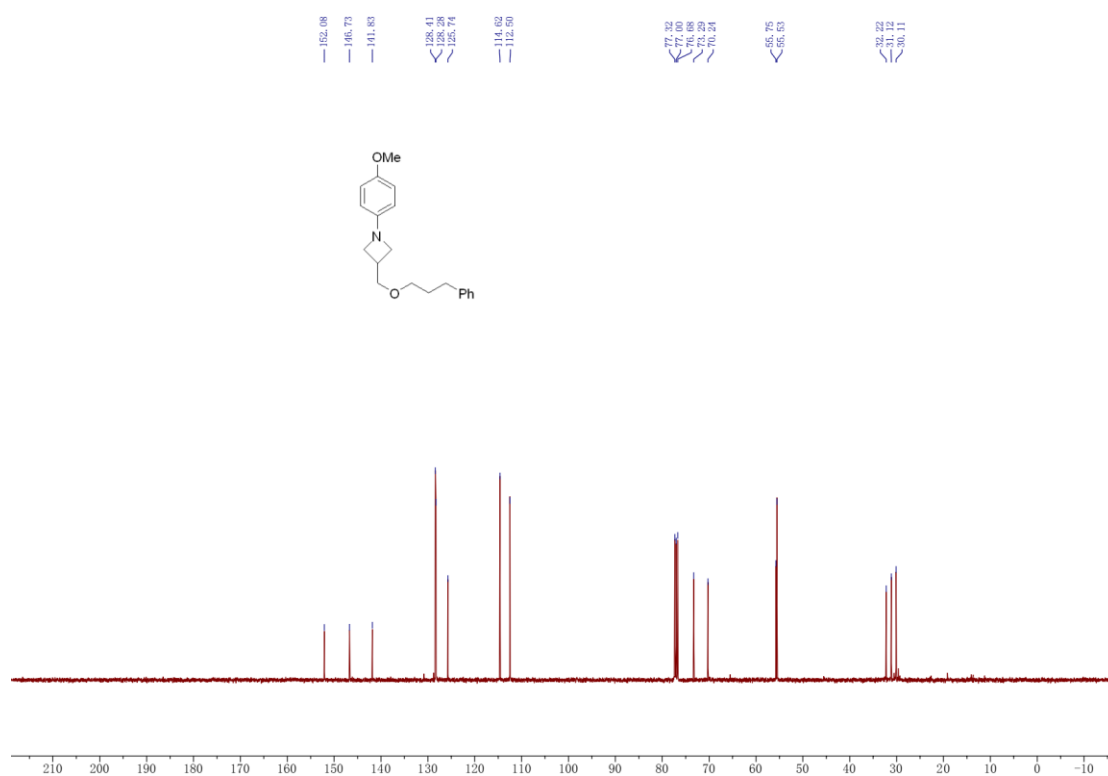
¹³C NMR spectrum of S35



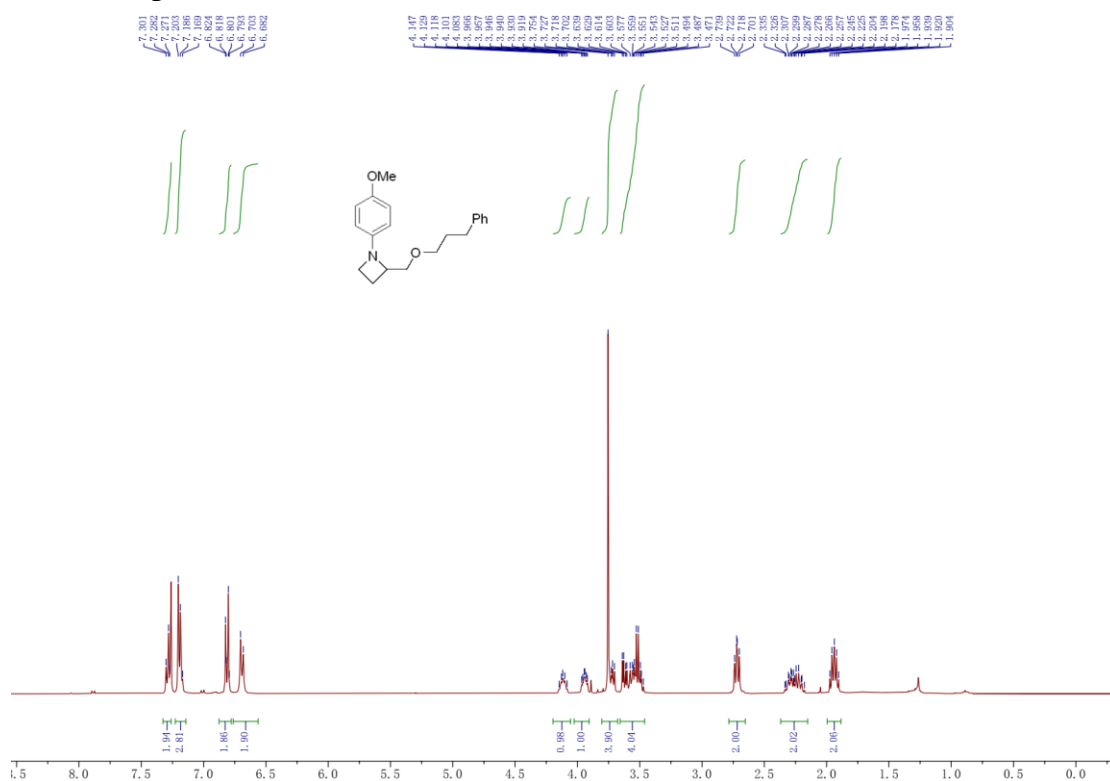
¹H NMR spectrum of 9



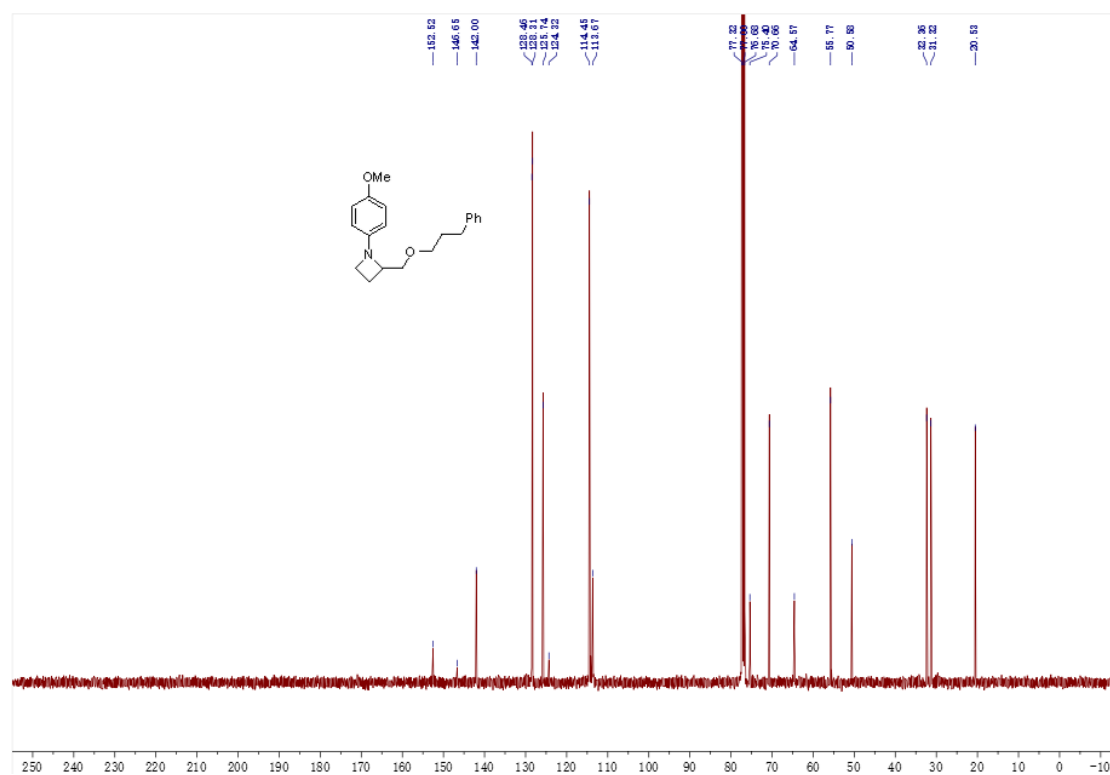
¹³C NMR spectrum of 9



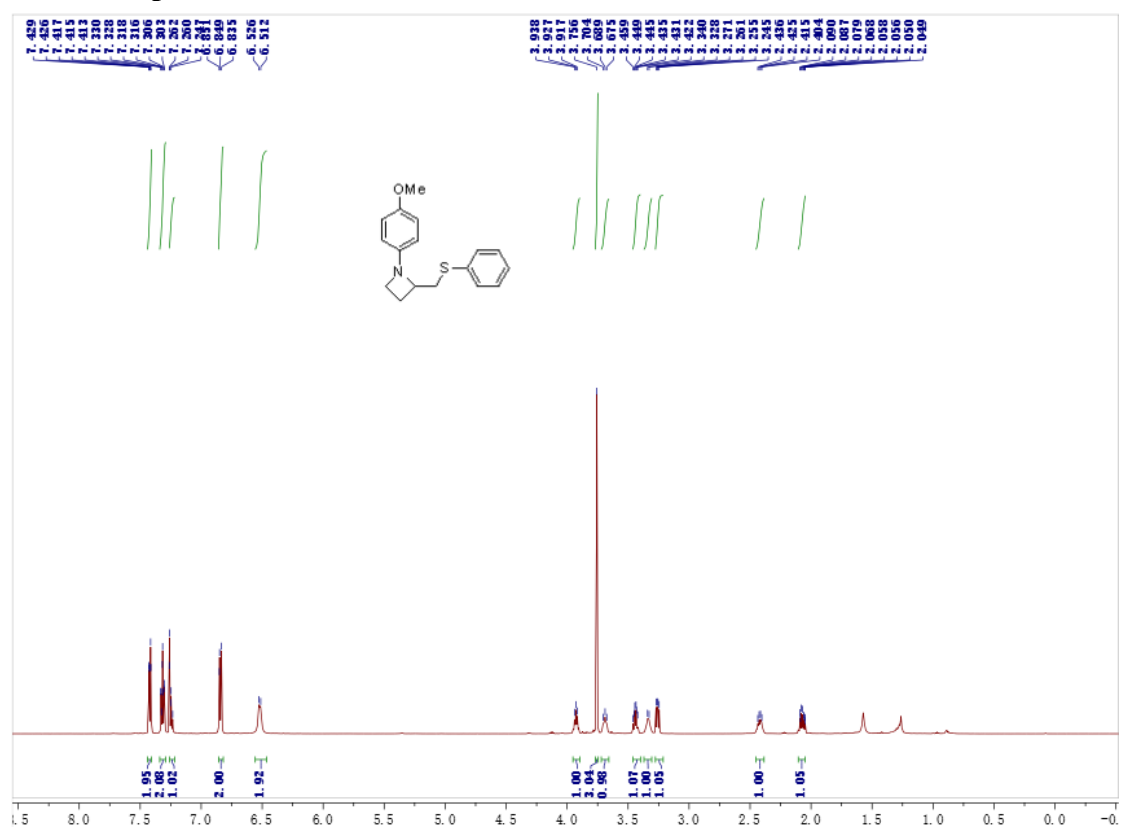
¹H NMR spectrum of 12



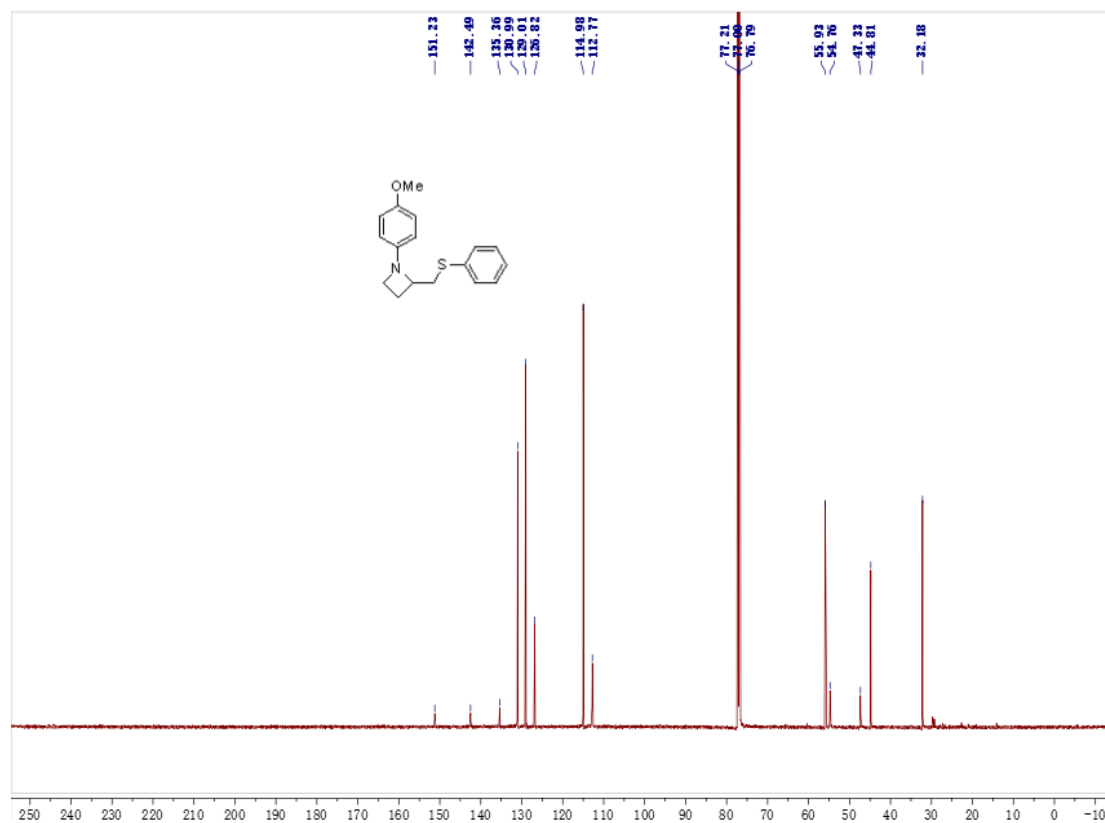
¹³C NMR spectrum of 12



¹H NMR spectrum of 13



¹³C NMR spectrum of 13



Chemical structure: COc1ccc(cc1)N2CCOC(C2)Cc3ccccc3

¹H NMR spectrum (CDCl₃) showing peaks from 0 to 8.5 ppm. The spectrum includes integration values and a chemical structure of the compound.

Chemical structure: COc1ccc(cc1)N2CCOC(C2)Cc3ccccc3

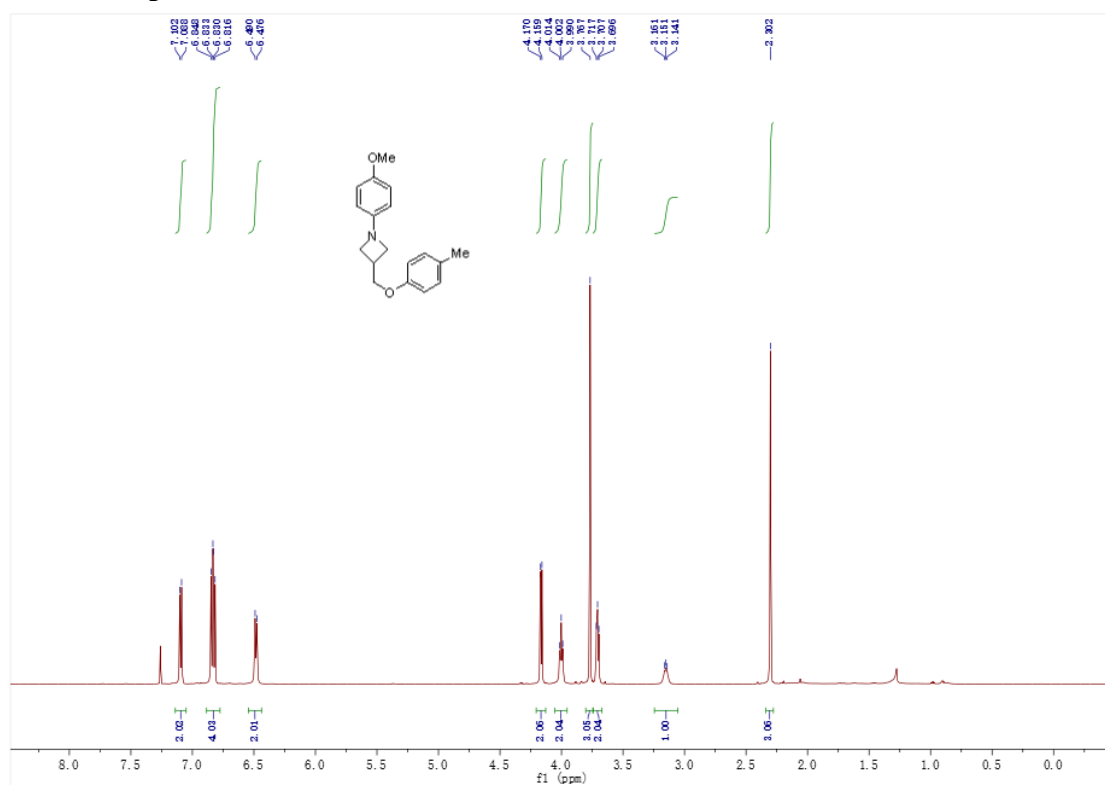
Integration values (from left to right): 4.96, 2.01, 2.06, 2.01, 2.08, 2.08, 2.01, 1.00.

Peak list (ppm): 7.54, 7.51, 7.49, 7.47, 7.45, 7.43, 7.41, 7.39, 7.37, 7.35, 7.33, 7.31, 7.29, 7.27, 7.25, 7.23, 7.21, 7.19, 7.17, 7.15, 7.13, 7.11, 7.09, 7.07, 7.05, 7.03, 7.01, 6.99, 6.97, 6.95, 6.93, 6.91, 6.89, 6.87, 6.85, 6.83, 6.81, 6.79, 6.77, 6.75, 6.73, 6.71, 6.69, 6.67, 6.65, 6.63, 6.61, 6.59, 6.57, 6.55, 6.53, 6.51, 6.49, 6.47, 6.45, 6.43, 6.41, 6.39, 6.37, 6.35, 6.33, 6.31, 6.29, 6.27, 6.25, 6.23, 6.21, 6.19, 6.17, 6.15, 6.13, 6.11, 6.09, 6.07, 6.05, 6.03, 6.01, 5.99, 5.97, 5.95, 5.93, 5.91, 5.89, 5.87, 5.85, 5.83, 5.81, 5.79, 5.77, 5.75, 5.73, 5.71, 5.69, 5.67, 5.65, 5.63, 5.61, 5.59, 5.57, 5.55, 5.53, 5.51, 5.49, 5.47, 5.45, 5.43, 5.41, 5.39, 5.37, 5.35, 5.33, 5.31, 5.29, 5.27, 5.25, 5.23, 5.21, 5.19, 5.17, 5.15, 5.13, 5.11, 5.09, 5.07, 5.05, 5.03, 5.01, 4.99, 4.97, 4.95, 4.93, 4.91, 4.89, 4.87, 4.85, 4.83, 4.81, 4.79, 4.77, 4.75, 4.73, 4.71, 4.69, 4.67, 4.65, 4.63, 4.61, 4.59, 4.57, 4.55, 4.53, 4.51, 4.49, 4.47, 4.45, 4.43, 4.41, 4.39, 4.37, 4.35, 4.33, 4.31, 4.29, 4.27, 4.25, 4.23, 4.21, 4.19, 4.17, 4.15, 4.13, 4.11, 4.09, 4.07, 4.05, 4.03, 4.01, 3.99, 3.97, 3.95, 3.93, 3.91, 3.89, 3.87, 3.85, 3.83, 3.81, 3.79, 3.77, 3.75, 3.73, 3.71, 3.69, 3.67, 3.65, 3.63, 3.61, 3.59, 3.57, 3.55, 3.53, 3.51, 3.49, 3.47, 3.45, 3.43, 3.41, 3.39, 3.37, 3.35, 3.33, 3.31, 3.29, 3.27, 3.25, 3.23, 3.21, 3.19, 3.17, 3.15, 3.13, 3.11, 3.09, 3.07, 3.05, 3.03, 3.01, 2.99, 2.97, 2.95, 2.93, 2.91, 2.89, 2.87, 2.85, 2.83, 2.81, 2.79, 2.77, 2.75, 2.73, 2.71, 2.69, 2.67, 2.65, 2.63, 2.61, 2.59, 2.57, 2.55, 2.53, 2.51, 2.49, 2.47, 2.45, 2.43, 2.41, 2.39, 2.37, 2.35, 2.33, 2.31, 2.29, 2.27, 2.25, 2.23, 2.21, 2.19, 2.17, 2.15, 2.13, 2.11, 2.09, 2.07, 2.05, 2.03, 2.01, 1.99, 1.97, 1.95, 1.93, 1.91, 1.89, 1.87, 1.85, 1.83, 1.81, 1.79, 1.77, 1.75, 1.73, 1.71, 1.69, 1.67, 1.65, 1.63, 1.61, 1.59, 1.57, 1.55, 1.53, 1.51, 1.49, 1.47, 1.45, 1.43, 1.41, 1.39, 1.37, 1.35, 1.33, 1.31, 1.29, 1.27, 1.25, 1.23, 1.21, 1.19, 1.17, 1.15, 1.13, 1.11, 1.09, 1.07, 1.05, 1.03, 1.01, 0.99, 0.97, 0.95, 0.93, 0.91, 0.89, 0.87, 0.85, 0.83, 0.81, 0.79, 0.77, 0.75, 0.73, 0.71, 0.69, 0.67, 0.65, 0.63, 0.61, 0.59, 0.57, 0.55, 0.53, 0.51, 0.49, 0.47, 0.45, 0.43, 0.41, 0.39, 0.37, 0.35, 0.33, 0.31, 0.29, 0.27, 0.25, 0.23, 0.21, 0.19, 0.17, 0.15, 0.13, 0.11, 0.09, 0.07, 0.05, 0.03, 0.01, 0.99, 0.97, 0.95, 0.93, 0.91, 0.89, 0.87, 0.85, 0.83, 0.81, 0.79, 0.77, 0.75, 0.73, 0.71, 0.69, 0.67, 0.65, 0.63, 0.61, 0.59, 0.57, 0.55, 0.53, 0.51, 0.49, 0.47, 0.45, 0.43, 0.41, 0.39, 0.37, 0.35, 0.33, 0.31, 0.29, 0.27, 0.25, 0.23, 0.21, 0.19, 0.17, 0.15, 0.13, 0.11, 0.09, 0.07, 0.05, 0.03, 0.01.

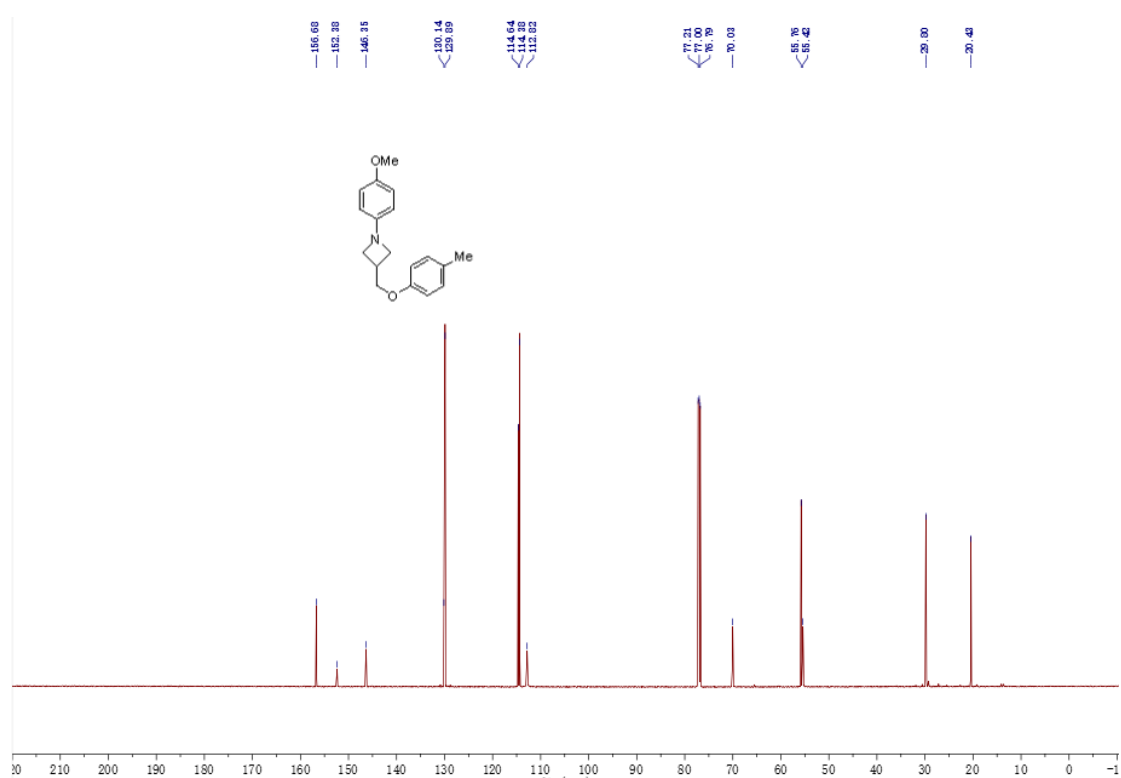
Chemical structure: COc1ccc(cc1)N2CCOC2Cc3ccccc3

¹³C NMR peaks (ppm): 152.13, 146.65, 138.17, 133.41, 127.60, 114.62, 112.96, 77.21, 77.00, 76.79, 76.58, 72.66, 55.70, 55.53, 30.12.

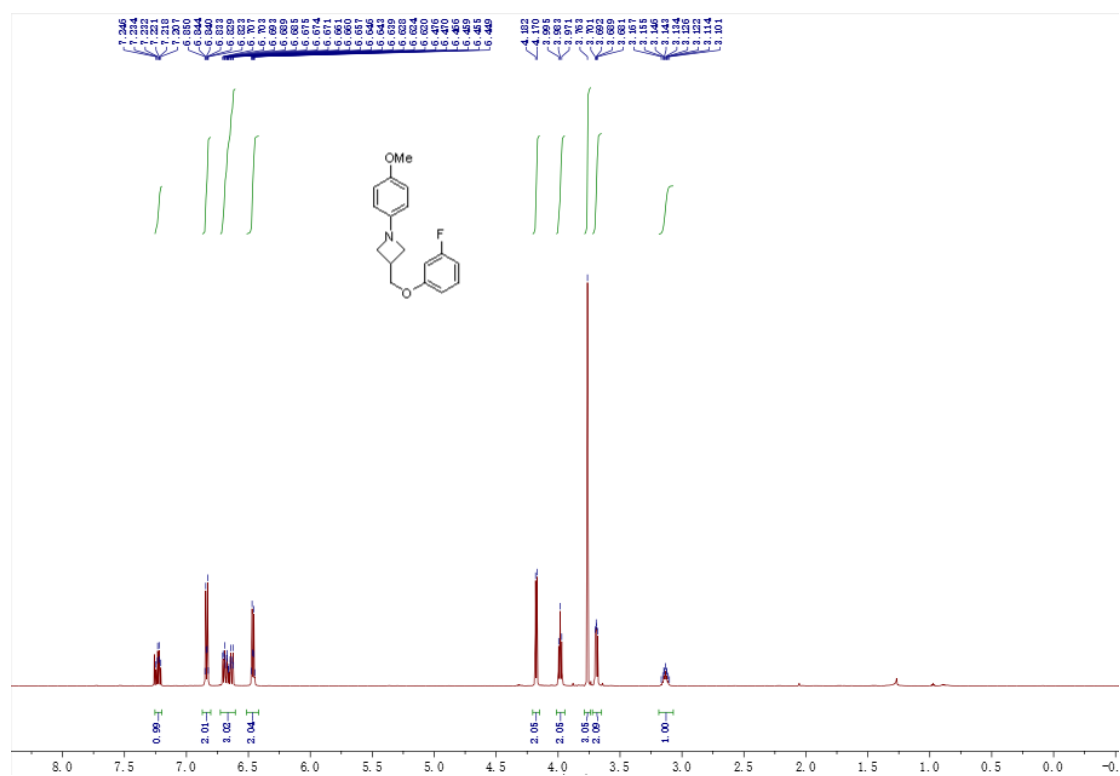
¹H NMR spectrum of 15



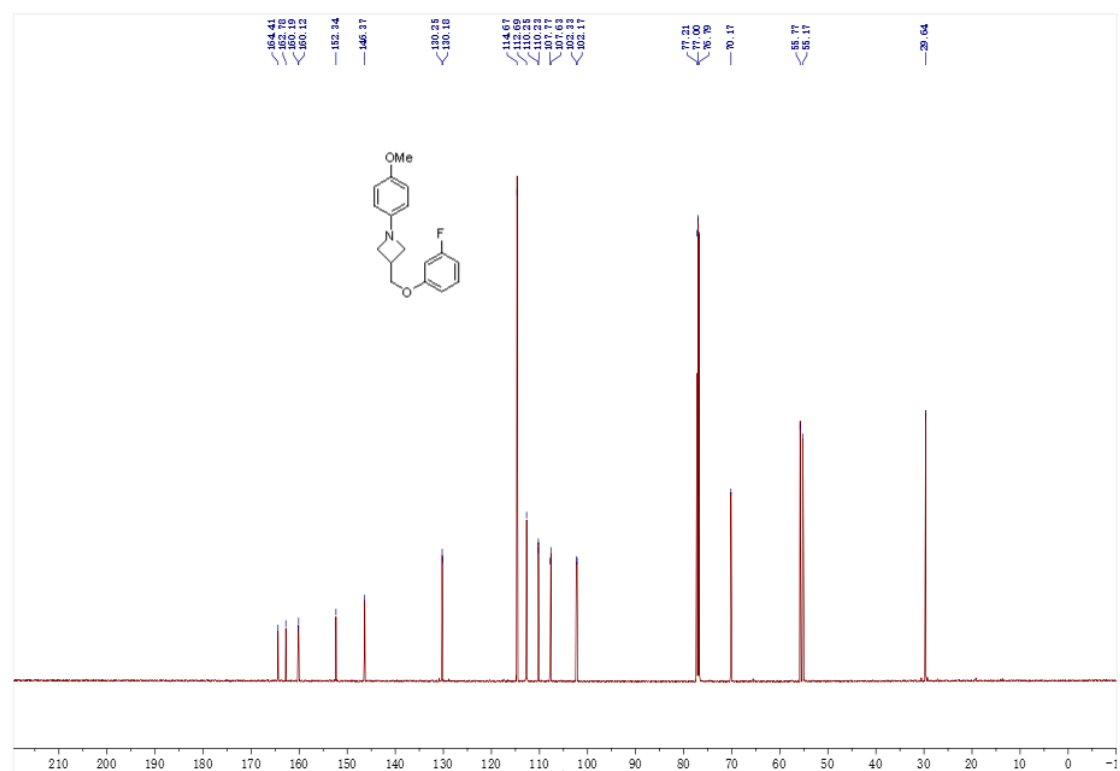
¹³C NMR spectrum of 15



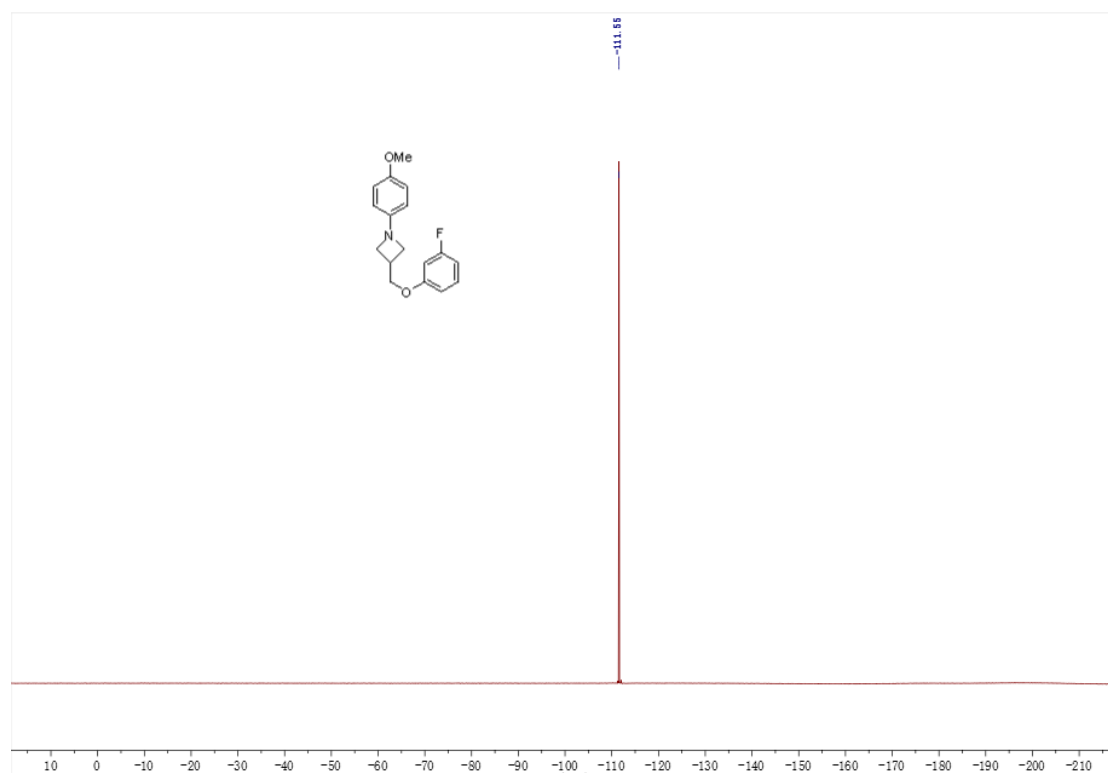
¹H NMR spectrum of 16



¹³C NMR spectrum of 16



^{19}F NMR spectrum of 16



Chemical structure: COc1ccc(cc1)N2CCCC2COc3ccc(I)cc3

¹H NMR spectrum (CDCl₃) showing peaks in the aromatic region (6.5-7.5 ppm) and aliphatic region (3.0-4.5 ppm). Integration values are provided below the peaks.

Peak list (ppm): 7.304, 7.291, 7.280, 7.273, 7.213, 7.043, 6.985, 6.965, 6.951, 6.871, 6.868, 6.843, 6.823, 6.817, 4.144, 4.135, 4.091, 4.079, 4.063, 3.963, 3.954, 3.143, 3.132, 3.122, 3.111, 3.102.

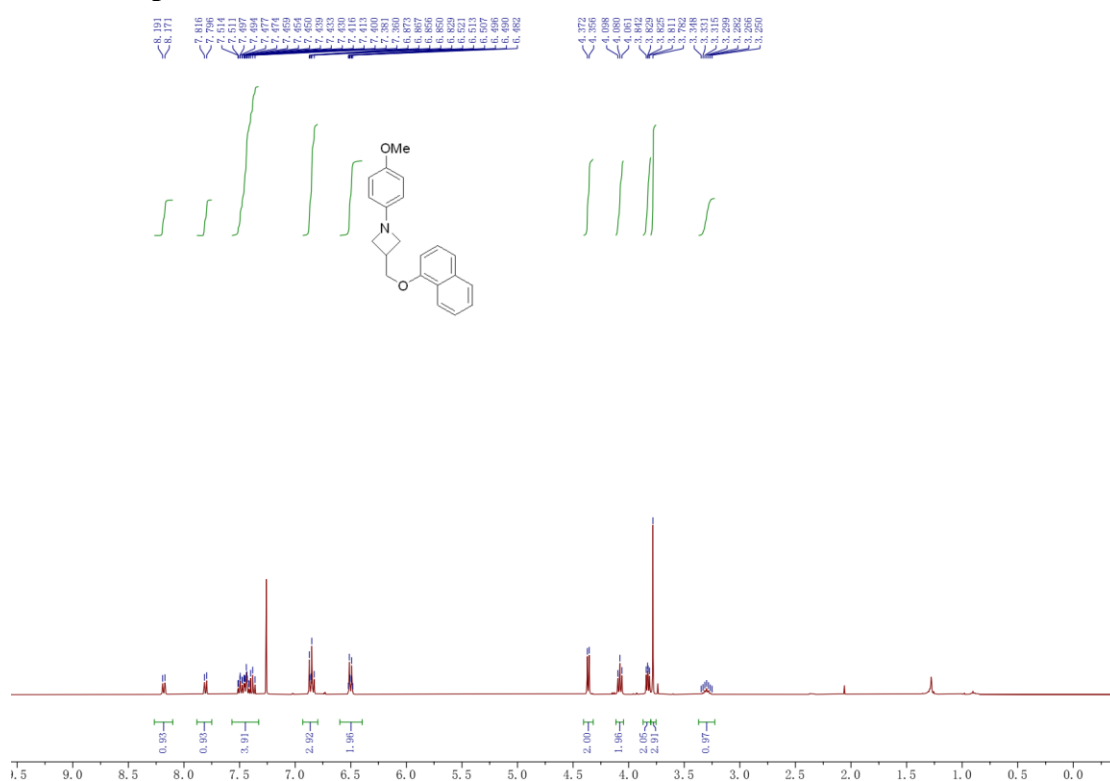
Integration values: 1.96, 1.08, 1.08, 1.97, 2.01, 2.09, 2.03, 2.03, 1.00.

Chemical structure of the compound is shown above the spectrum. The structure is 1-(4-methoxyphenyl)-2-(4-iodophenoxy)pyrrolidine.

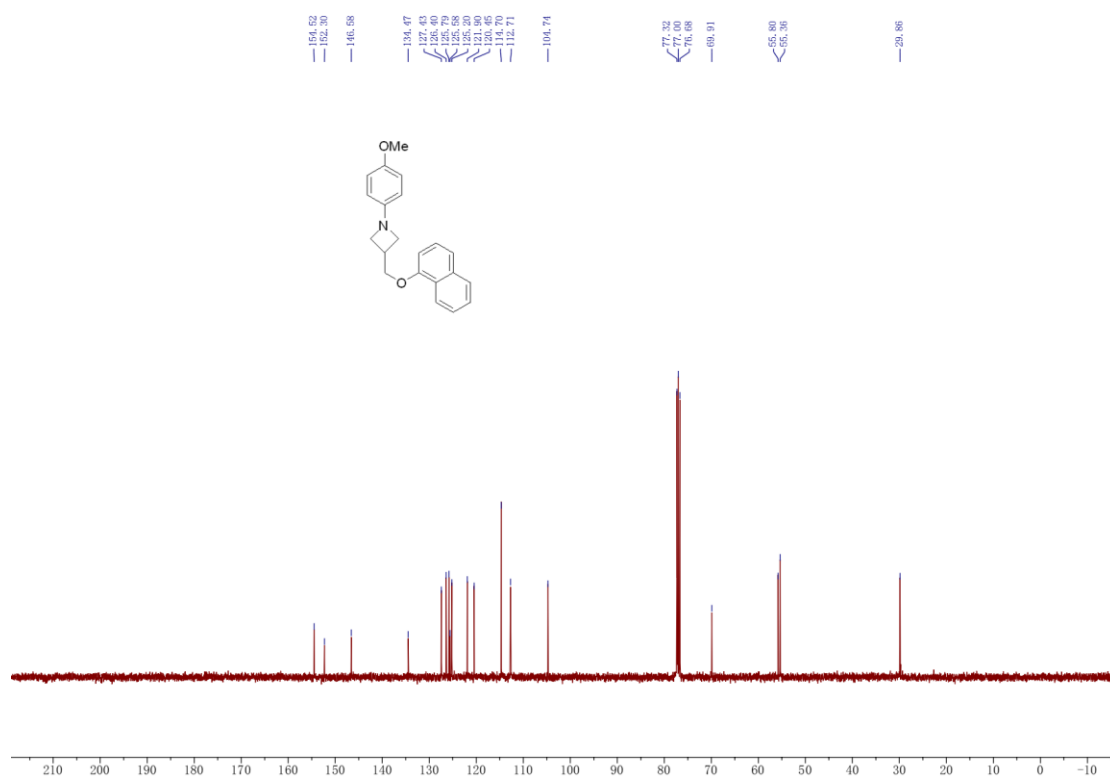
¹H NMR spectrum (CDCl₃) of the compound. The x-axis represents chemical shift in ppm, ranging from 0 to 210. The spectrum shows several peaks corresponding to the structure:

- ~3.8 ppm (s, 3H, OMe)
- ~7.1 ppm (m, 4H, aromatic)
- ~7.4 ppm (m, 4H, aromatic)
- ~7.7 ppm (s, 2H, aromatic)
- ~12.7 ppm (m, 2H, aromatic)
- ~13.0 ppm (m, 2H, aromatic)
- ~13.2 ppm (m, 2H, aromatic)
- ~13.4 ppm (m, 2H, aromatic)
- ~13.6 ppm (m, 2H, aromatic)
- ~13.8 ppm (m, 2H, aromatic)
- ~14.0 ppm (m, 2H, aromatic)
- ~14.2 ppm (m, 2H, aromatic)
- ~14.4 ppm (m, 2H, aromatic)
- ~14.6 ppm (m, 2H, aromatic)
- ~14.8 ppm (m, 2H, aromatic)
- ~15.0 ppm (m, 2H, aromatic)
- ~15.2 ppm (m, 2H, aromatic)
- ~15.4 ppm (m, 2H, aromatic)
- ~15.6 ppm (m, 2H, aromatic)
- ~15.8 ppm (m, 2H, aromatic)
- ~16.0 ppm (m, 2H, aromatic)
- ~16.2 ppm (m, 2H, aromatic)
- ~16.4 ppm (m, 2H, aromatic)
- ~16.6 ppm (m, 2H, aromatic)
- ~16.8 ppm (m, 2H, aromatic)
- ~17.0 ppm (m, 2H, aromatic)
- ~17.2 ppm (m, 2H, aromatic)
- ~17.4 ppm (m, 2H, aromatic)
- ~17.6 ppm (m, 2H, aromatic)
- ~17.8 ppm (m, 2H, aromatic)
- ~18.0 ppm (m, 2H, aromatic)
- ~18.2 ppm (m, 2H, aromatic)
- ~18.4 ppm (m, 2H, aromatic)
- ~18.6 ppm (m, 2H, aromatic)
- ~18.8 ppm (m, 2H, aromatic)
- ~19.0 ppm (m, 2H, aromatic)
- ~19.2 ppm (m, 2H, aromatic)
- ~19.4 ppm (m, 2H, aromatic)
- ~19.6 ppm (m, 2H, aromatic)
- ~19.8 ppm (m, 2H, aromatic)
- ~20.0 ppm (m, 2H, aromatic)
- ~20.2 ppm (m, 2H, aromatic)
- ~20.4 ppm (m, 2H, aromatic)
- ~20.6 ppm (m, 2H, aromatic)
- ~20.8 ppm (m, 2H, aromatic)
- ~21.0 ppm (m, 2H, aromatic)

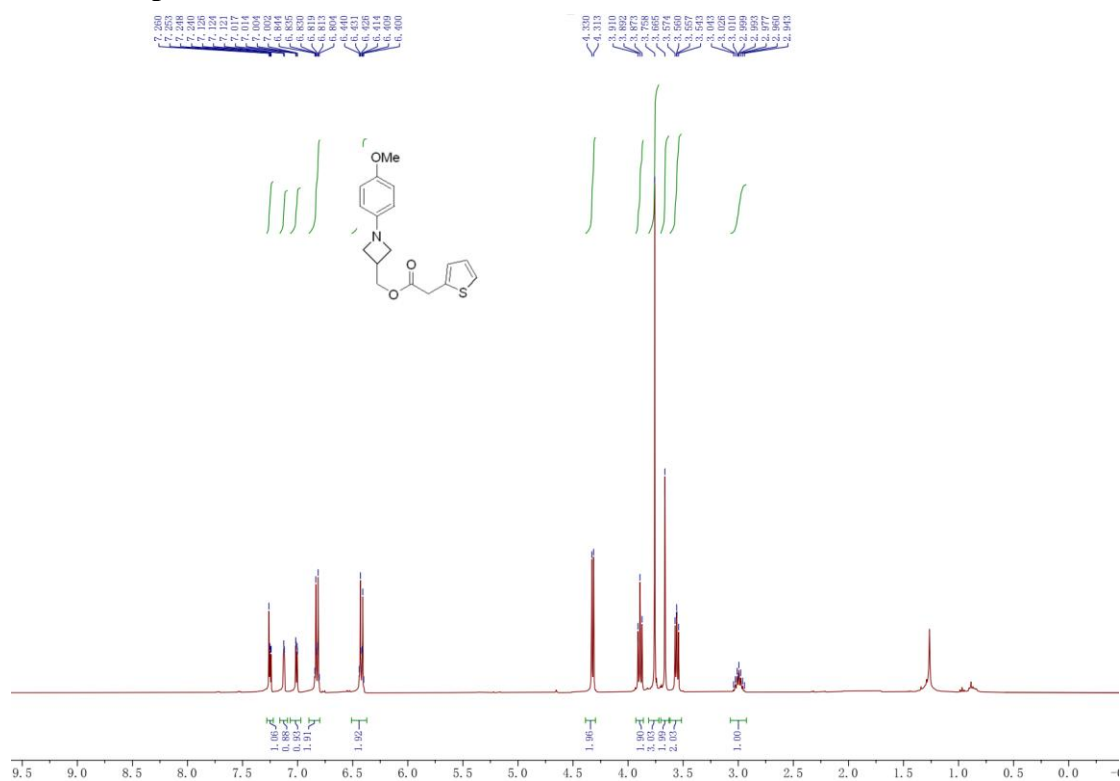
¹H NMR spectrum of 18



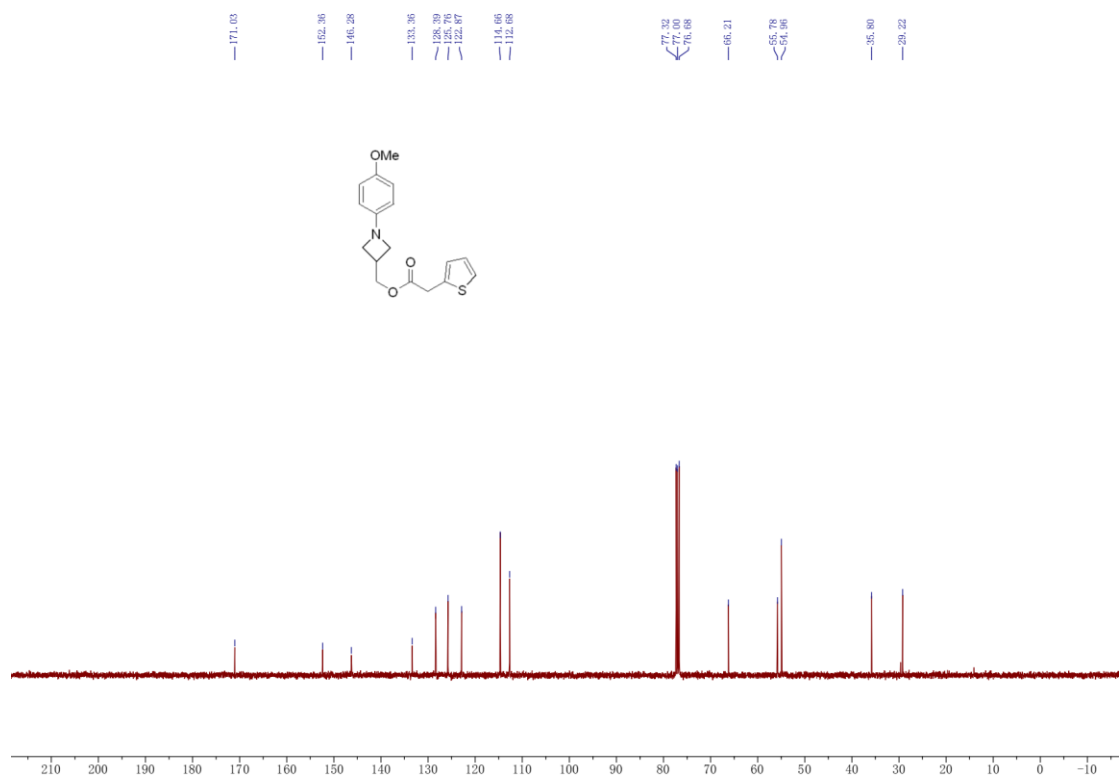
¹³C NMR spectrum of 18



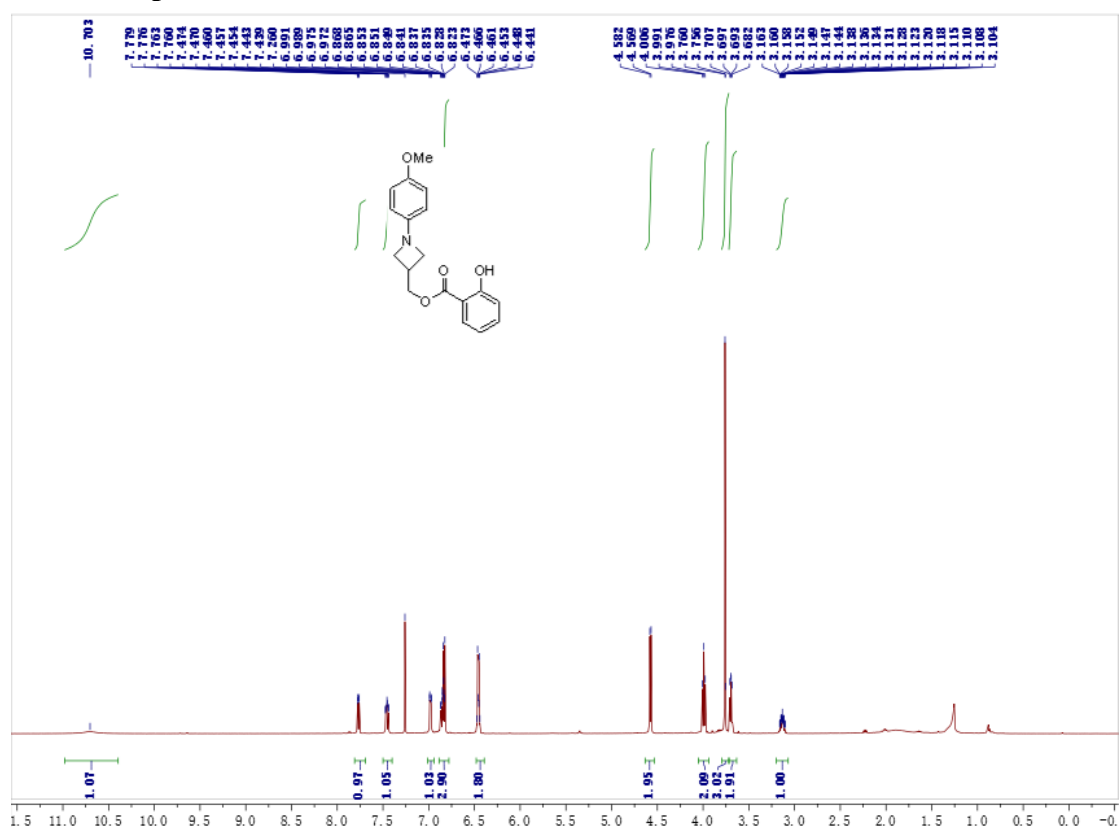
¹H NMR spectrum of 19



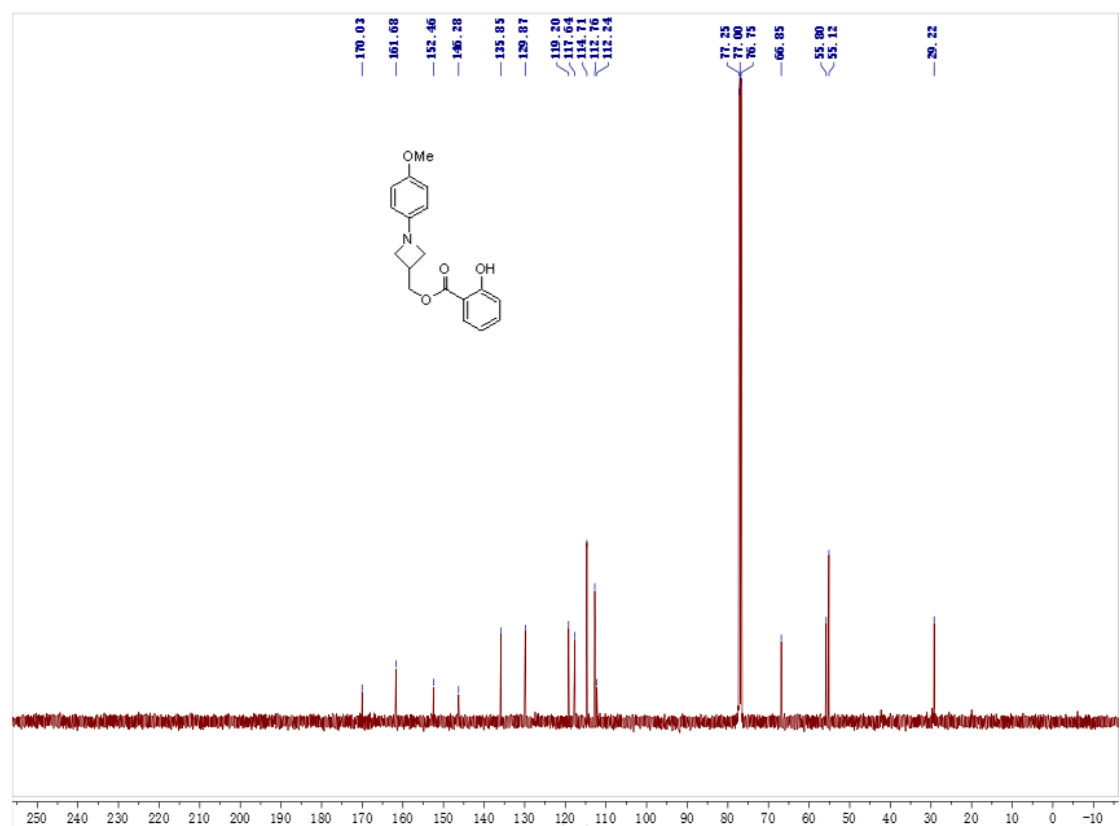
¹³C NMR spectrum of 19



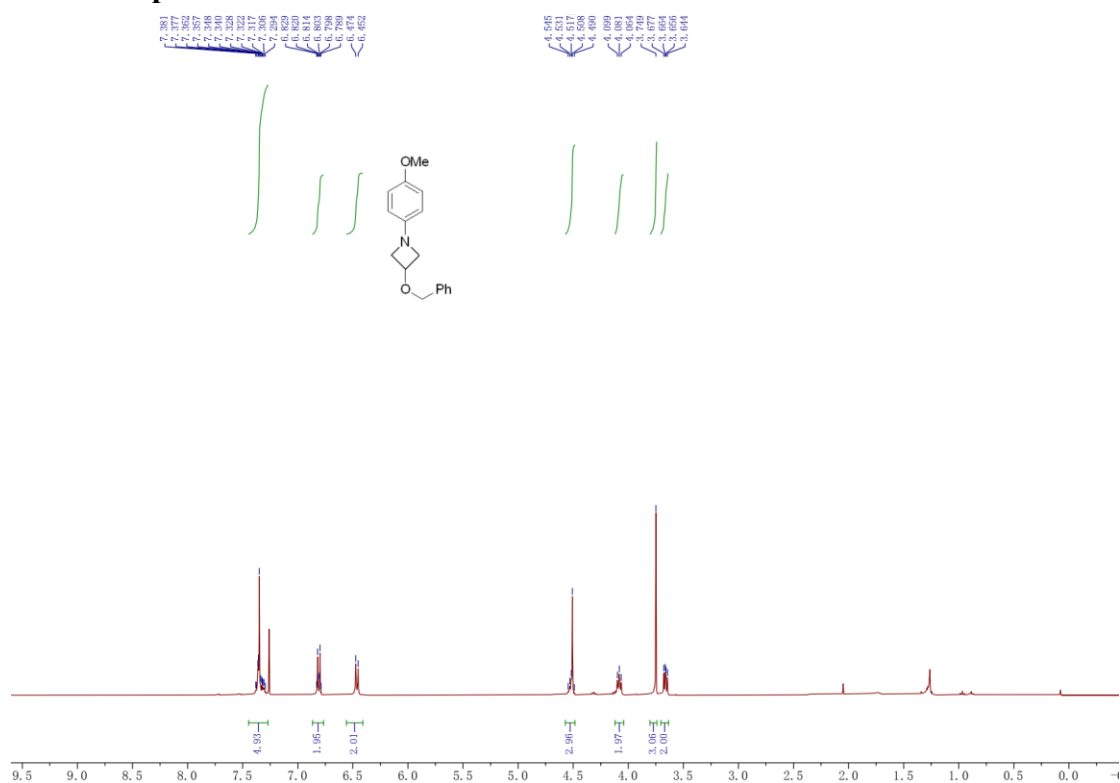
¹H NMR spectrum of 20



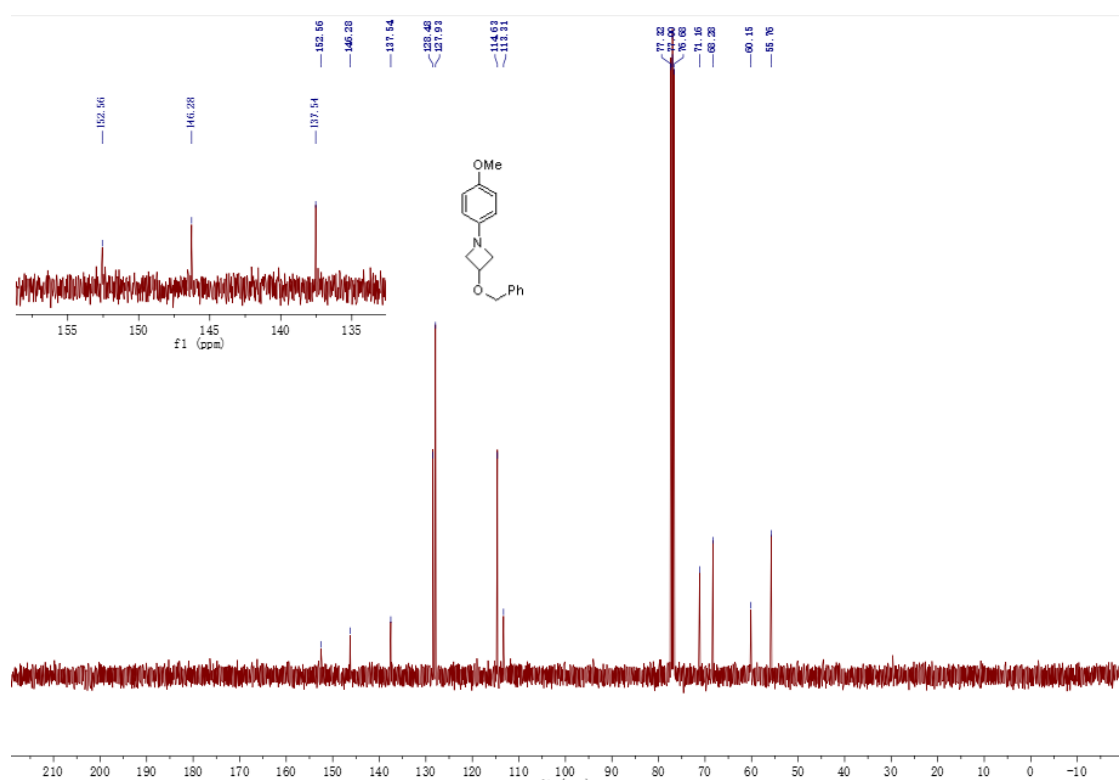
¹³C NMR spectrum of 20



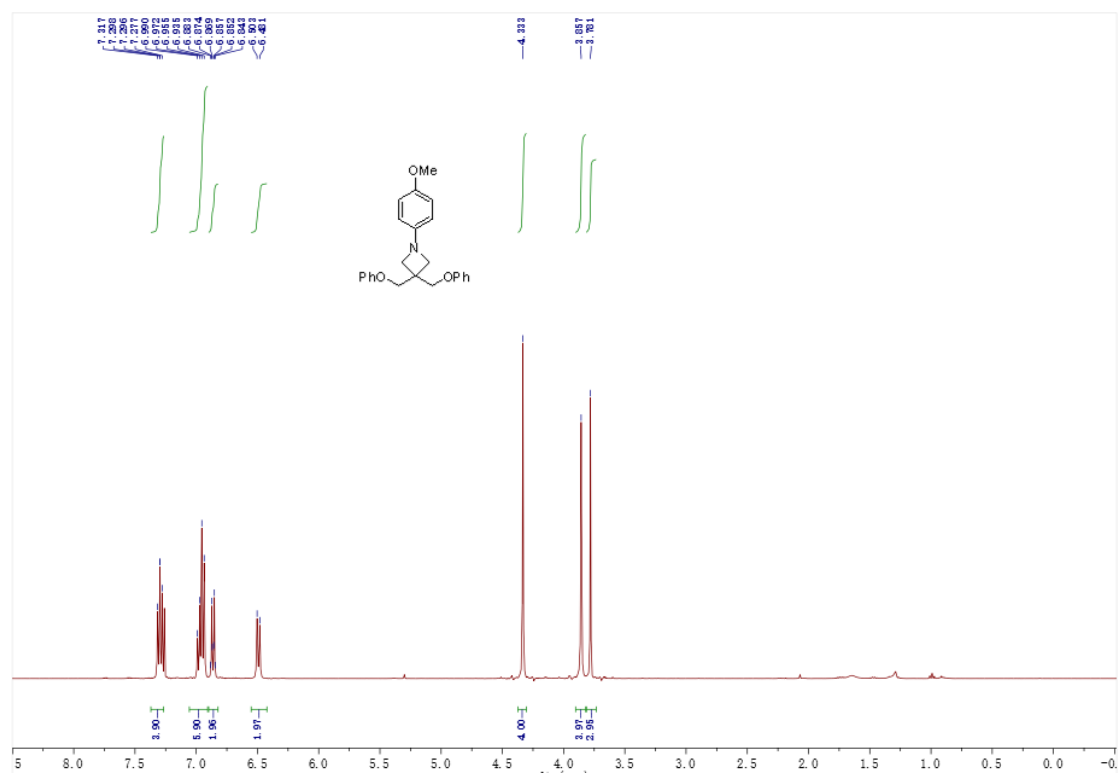
¹H NMR spectrum of 21



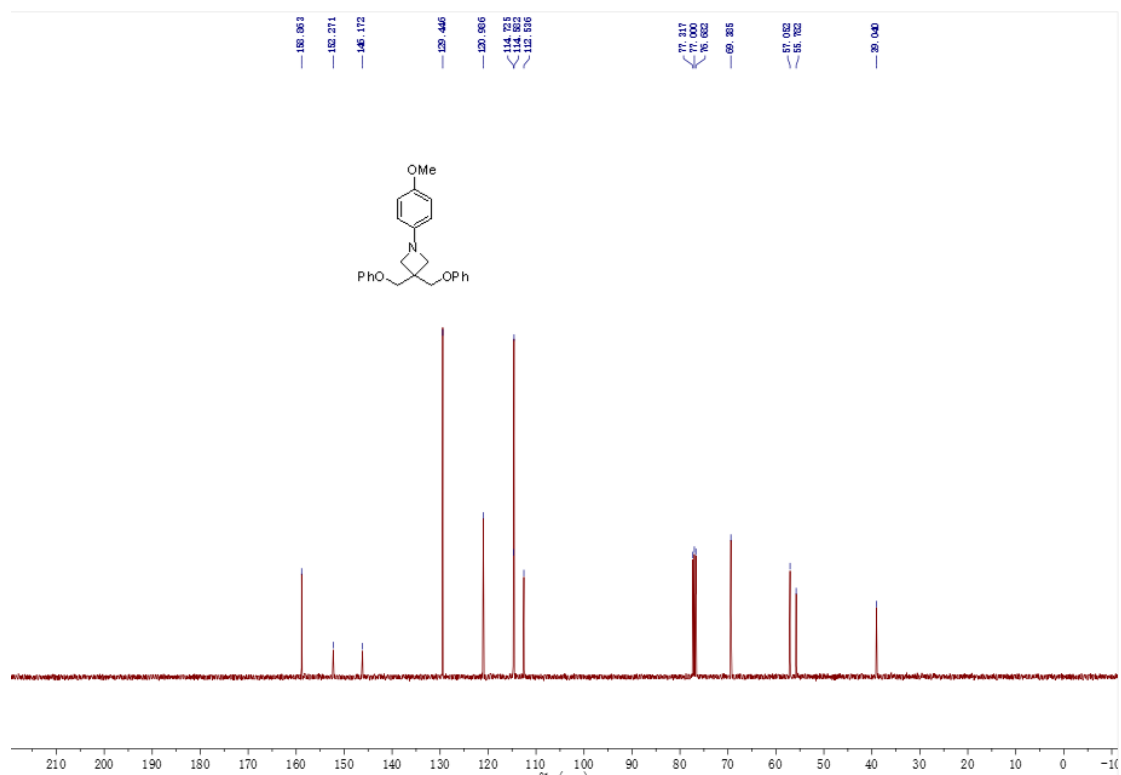
¹³C NMR spectrum of 21



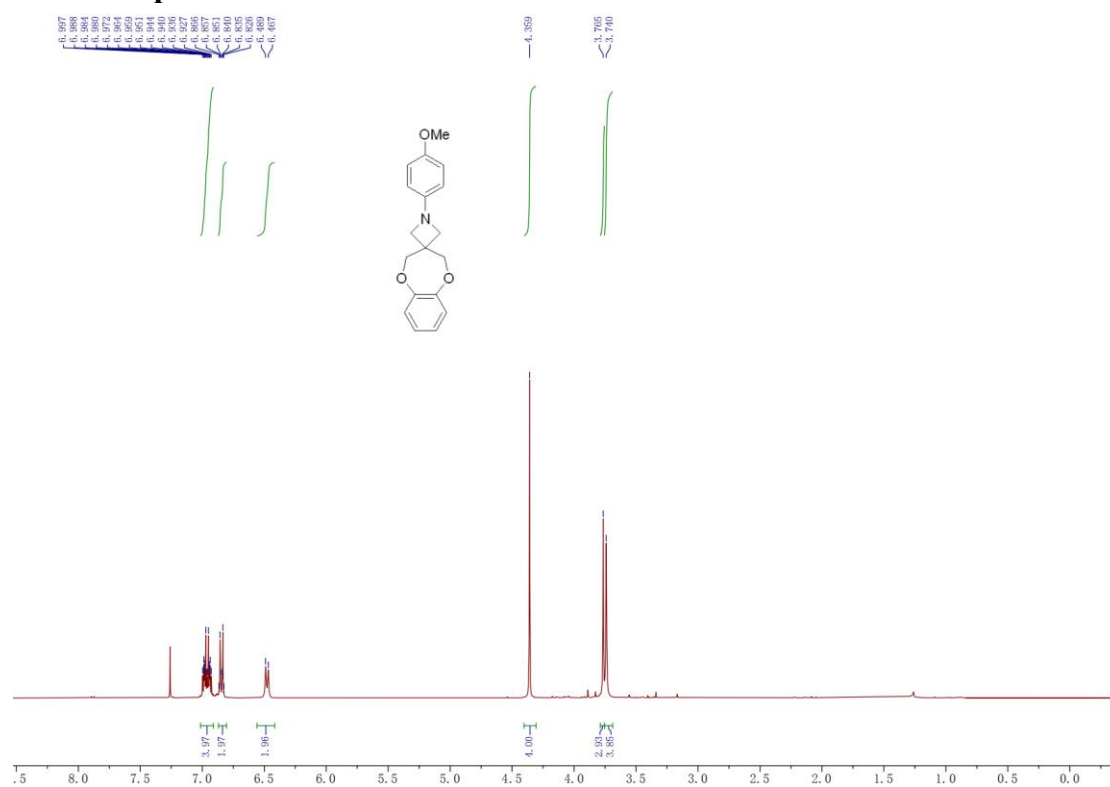
¹H NMR spectrum of 22



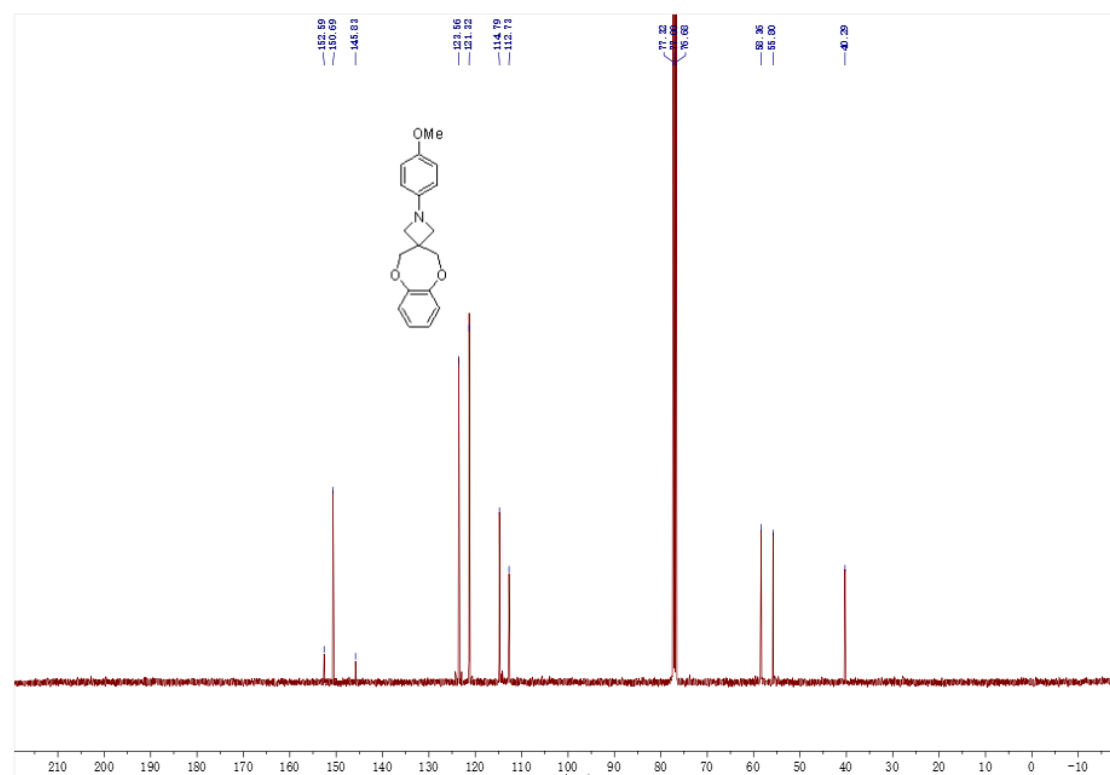
¹³C NMR spectrum of 22



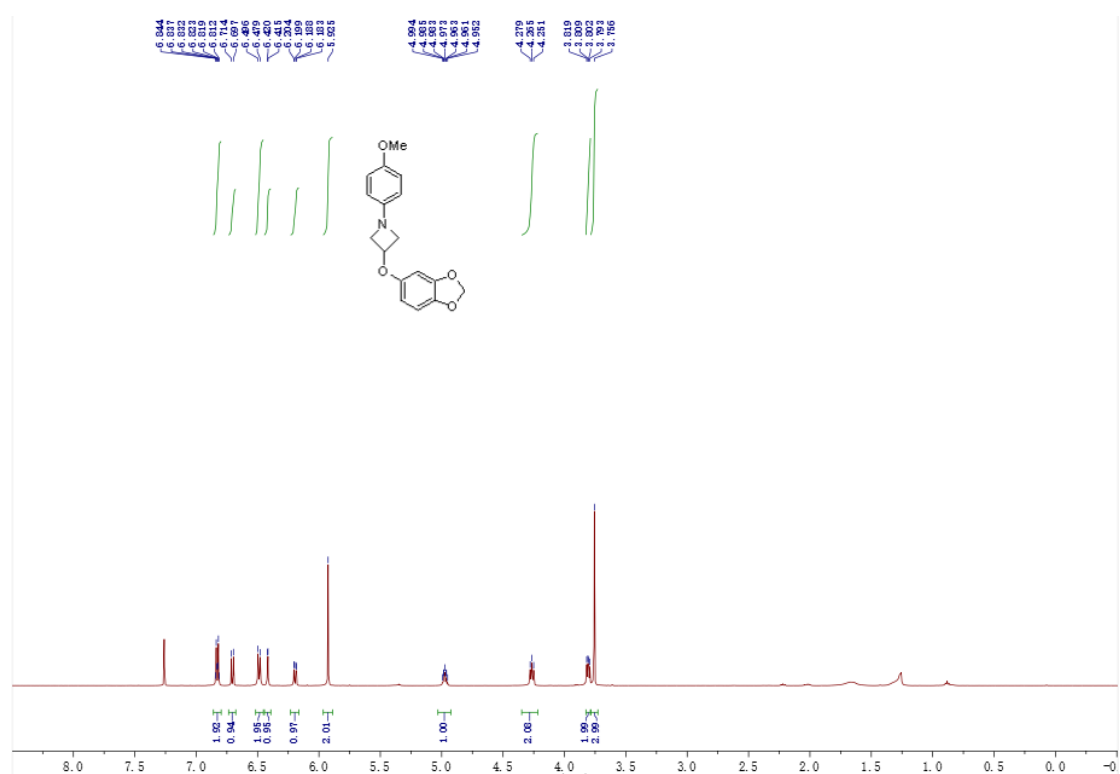
¹H NMR spectrum of 23



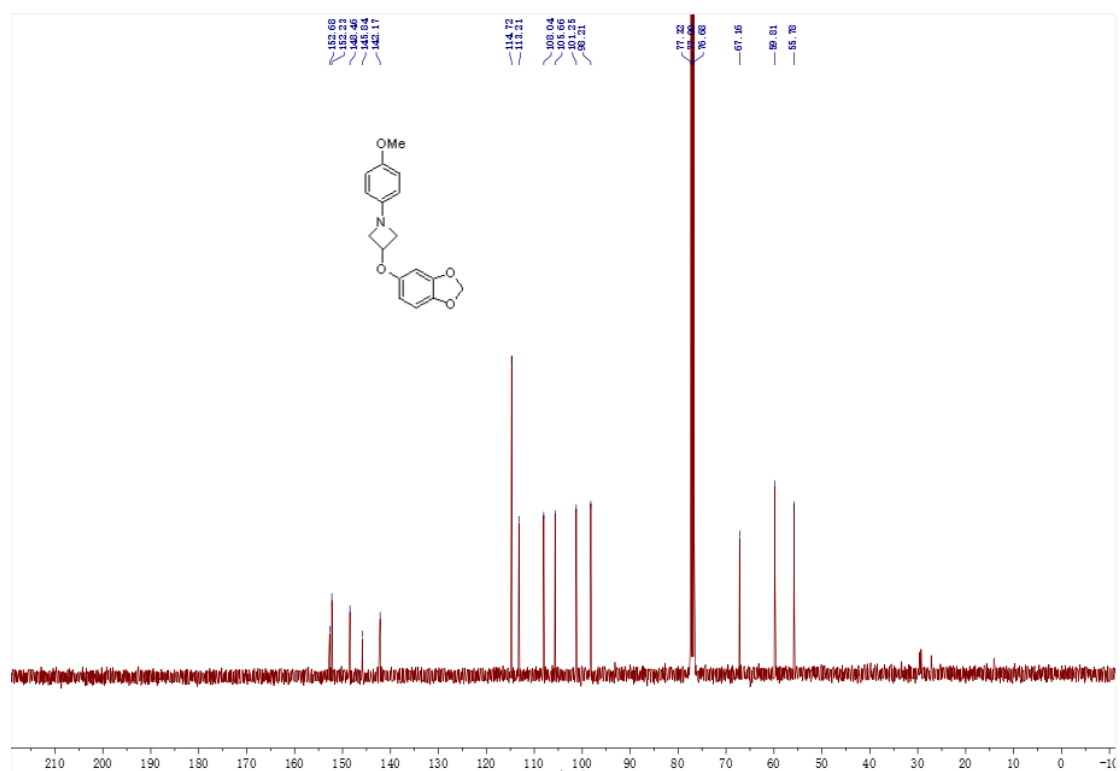
¹³C NMR spectrum of 23



¹H NMR spectrum of 24



¹³C NMR spectrum of 24



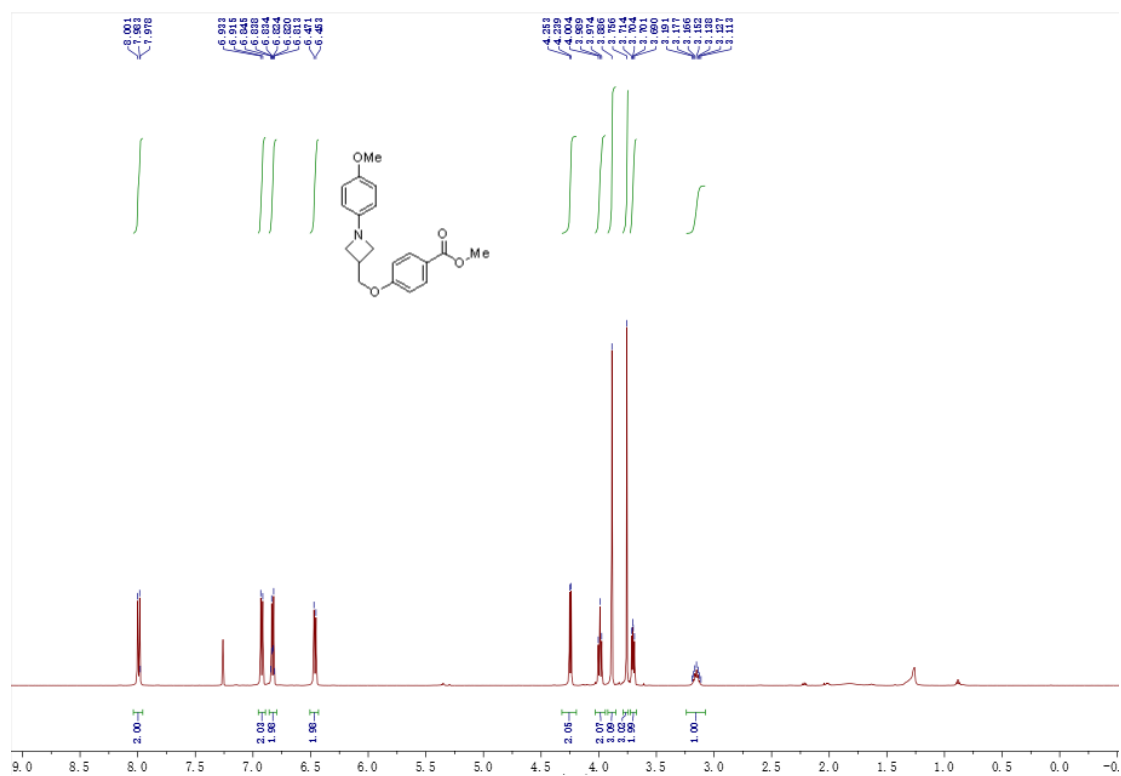
Chemical structure: COc1ccc(cc1)N2CCOC(C(C)C)CC(C)C2

¹H NMR spectrum (CDCl₃) showing peaks from 0 to 8 ppm. The spectrum includes aromatic protons (6.5-6.9 ppm), methoxy protons (3.8 ppm), sugar ring protons (3.2-3.8 ppm), anomeric proton (5.1 ppm), and dimethyl protons (1.0 ppm). Integration values are provided below the peaks.

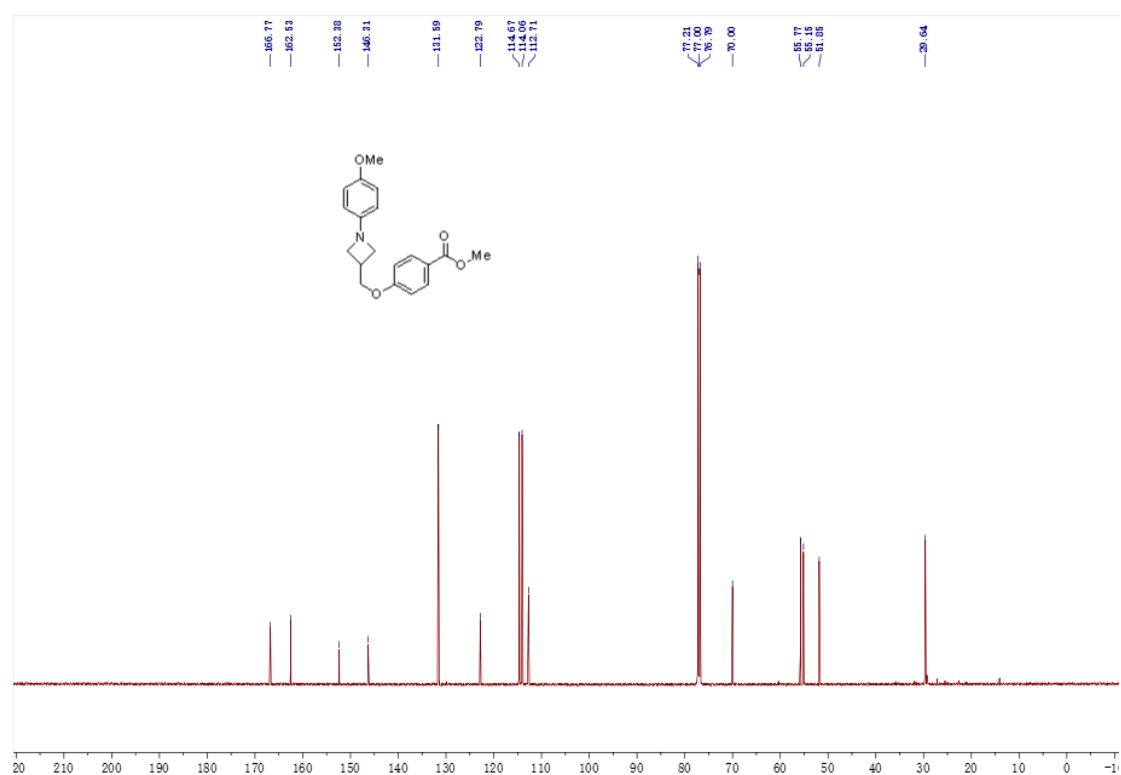
Chemical structure of 4-(4-methoxyphenyl)-1-(4,4,4-trimethyl-1-pentoxy)pyrrolidine is shown above the ¹³C NMR spectrum. The spectrum displays peaks corresponding to the structure, with the following chemical shifts (ppm) labeled above the peaks:

- 152.09
- 146.76
- 114.64
- 112.53
- 77.25
- 77.00
- 76.75
- 72.41
- 69.69
- 55.80
- 55.61
- 39.25
- 37.31
- 36.61
- 30.14
- 30.87
- 27.94
- 24.64
- 22.69
- 22.39
- 19.61

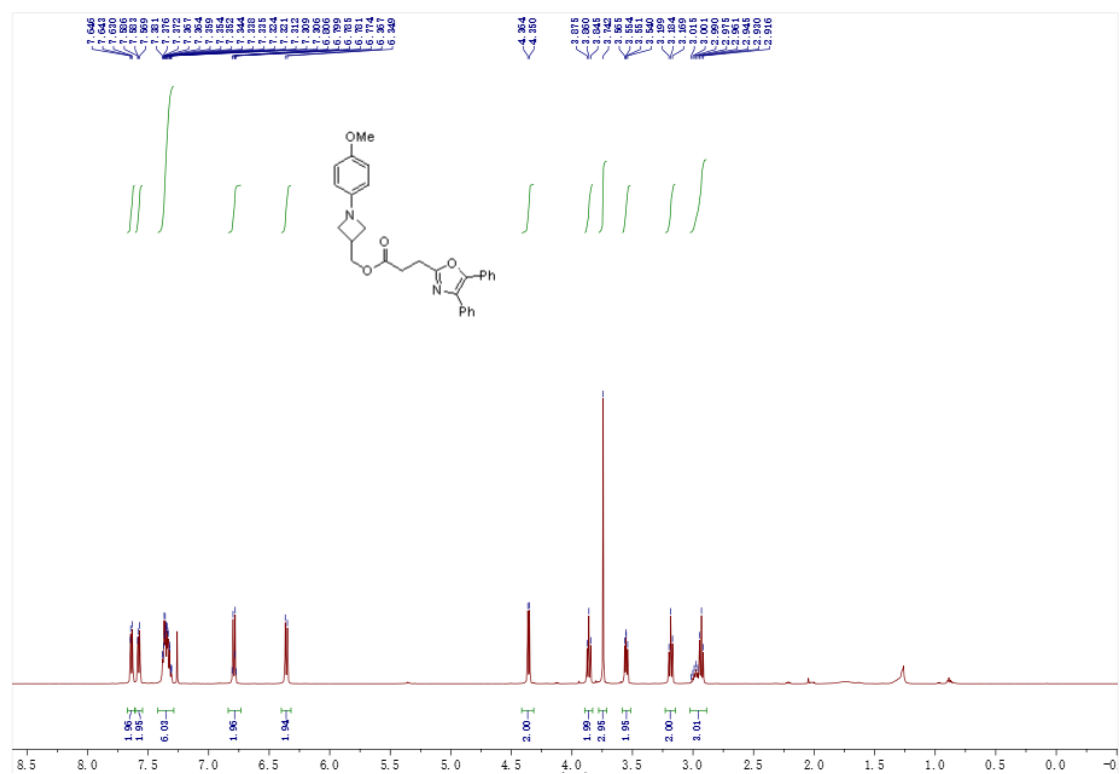
¹H NMR spectrum of 26



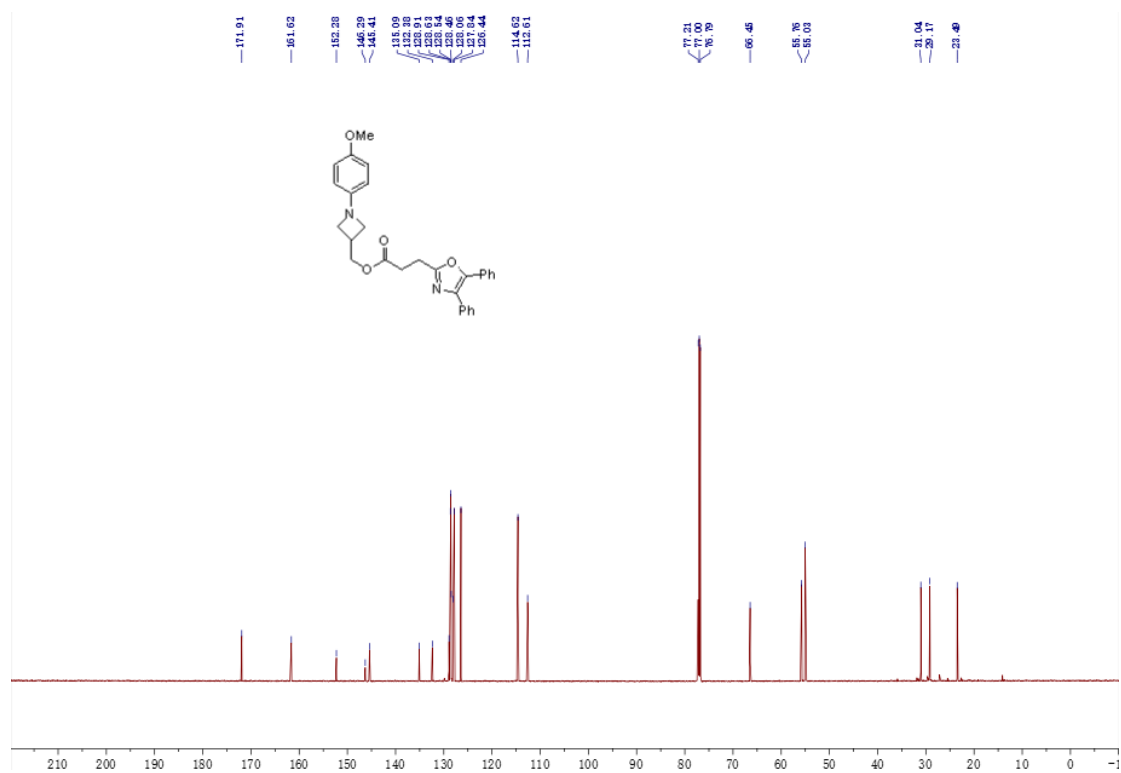
^{13}C NMR spectrum of 26



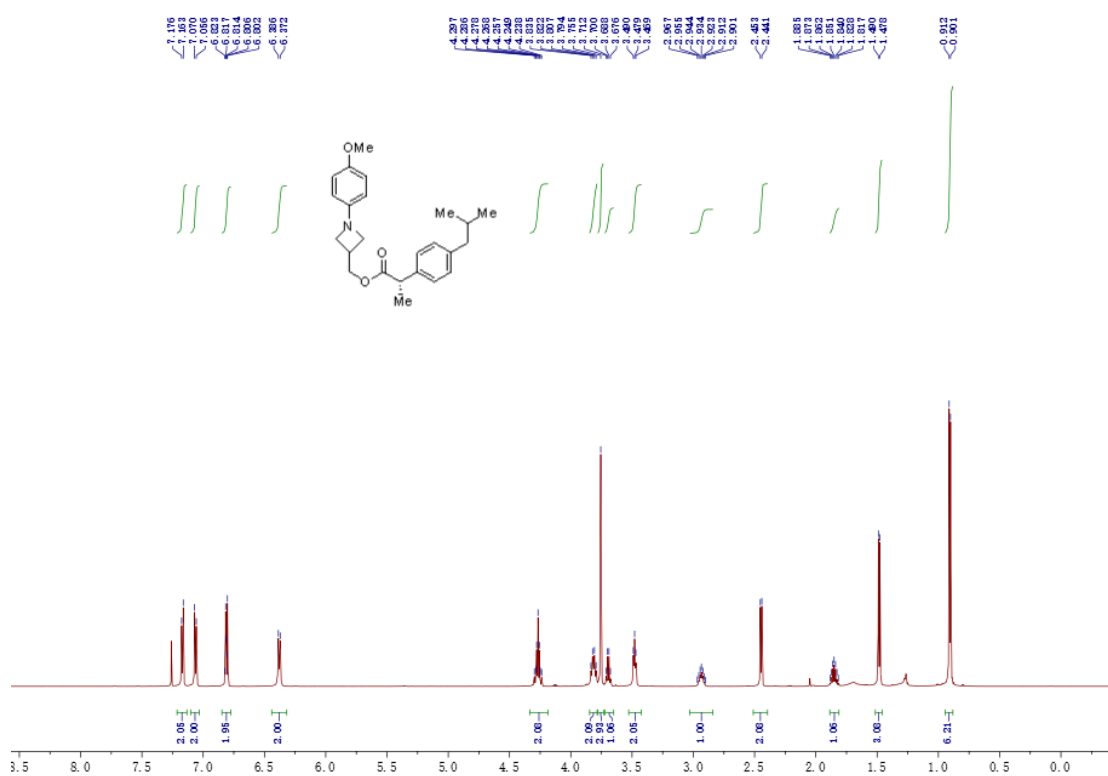
¹H NMR spectrum of 27



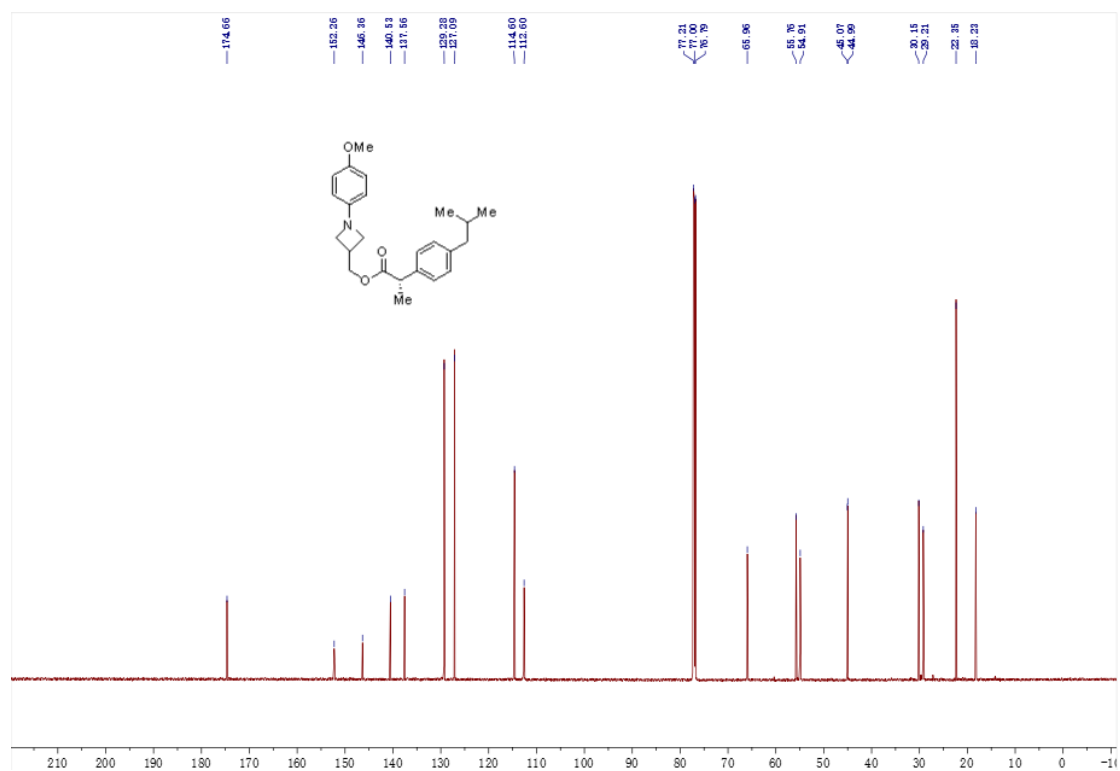
¹³C NMR spectrum of 27



¹H NMR spectrum of 28



¹³C NMR spectrum of 28



¹H NMR spectrum (CDCl₃) of compound 10. The spectrum shows peaks from 0 to 8 ppm. Aromatic and heterocyclic protons appear between 6.5 and 7.7 ppm. A methoxy singlet is at 3.8 ppm. A methine proton is at 3.6 ppm. A methyl group is at 2.3 ppm. Integration values are shown below the peaks.

Chemical structure of compound 10 is shown above the spectrum:

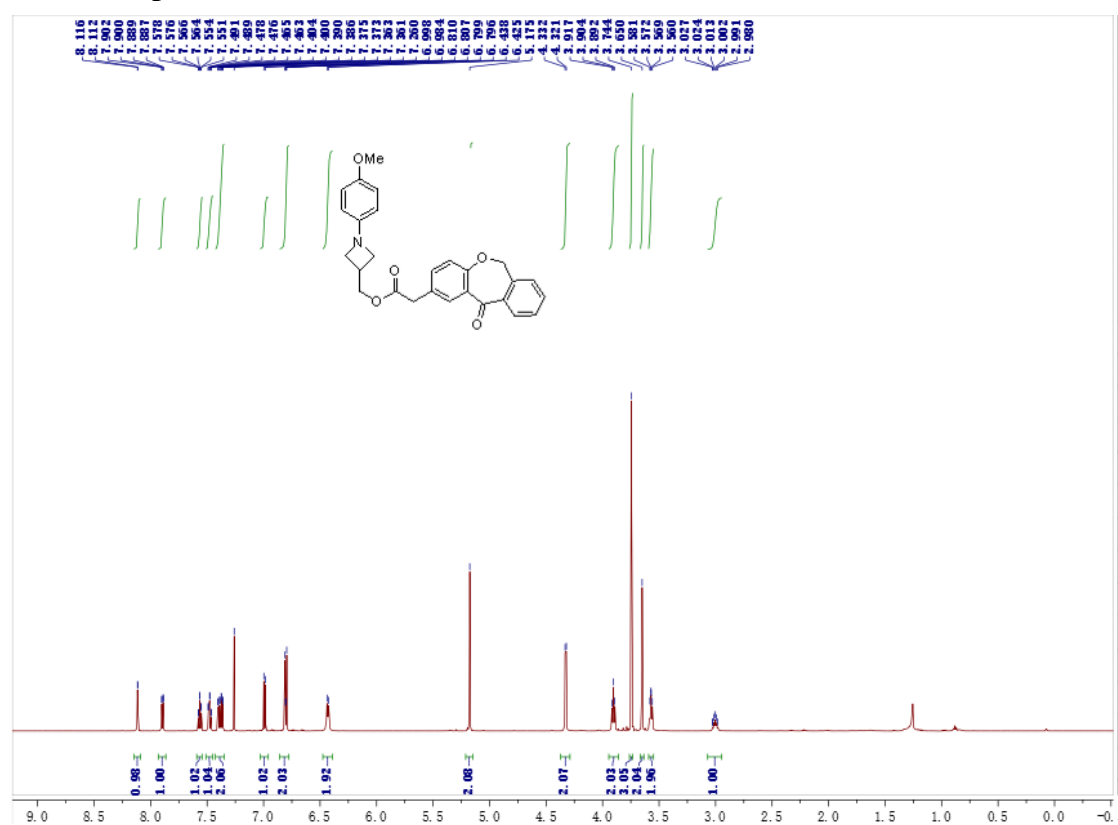
COc1ccc(cc1)N2CCOC2C(=O)Cc3c(C)c(C(=O)c4ccc(Cl)cc4)n5cc(OC)ccc5

Chemical structure of compound 10 is shown above the spectrum. The structure is a complex molecule featuring a central benzimidazole core. It includes a 4-methoxyphenyl group, a 4-chlorophenyl group, a 2-methoxyphenyl group, and a 2-methyl-2-oxoethyl group. The spectrum displays peaks corresponding to these various carbon environments.

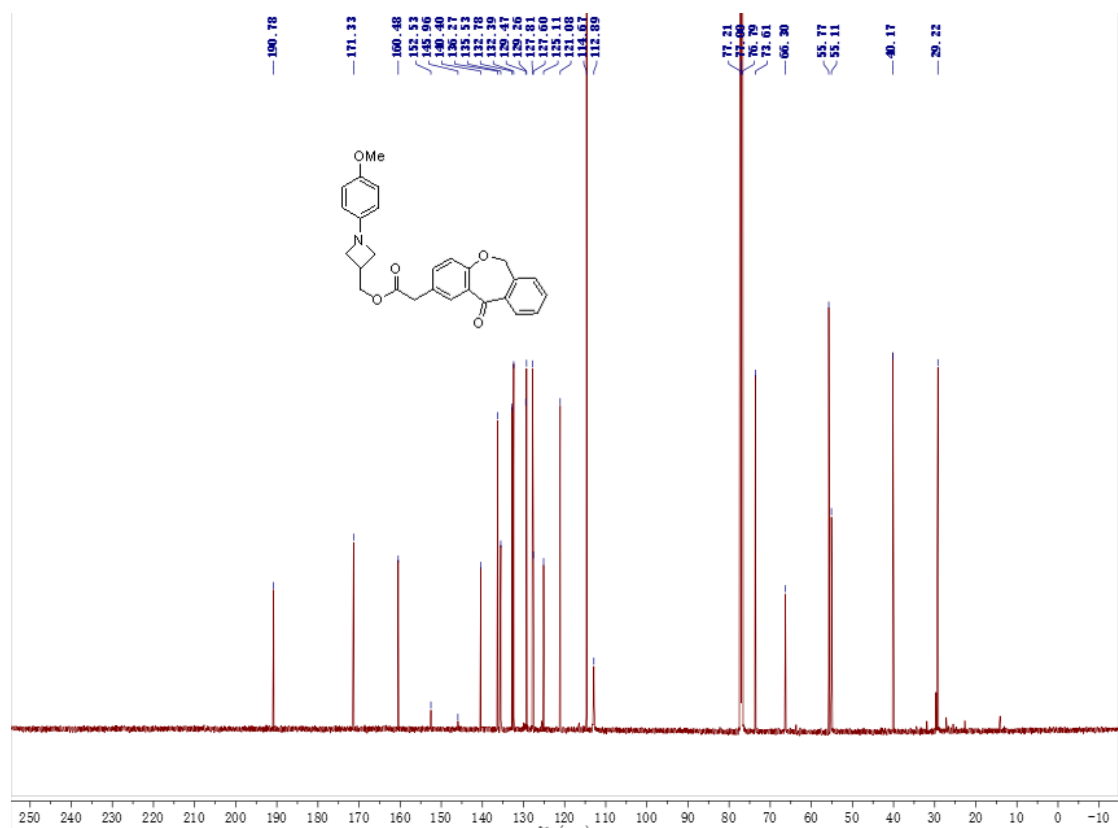
Peak list (ppm):

- 170.70
- 168.20
- 156.01
- 152.41
- 146.11
- 139.24
- 138.64
- 133.64
- 131.14
- 129.24
- 129.08
- 114.85
- 114.85
- 112.70
- 112.36
- 111.80
- 101.34
- 77.21
- 77.00
- 76.79
- 66.32
- 55.94
- 55.94
- 55.03
- 30.30
- 29.23
- 13.25

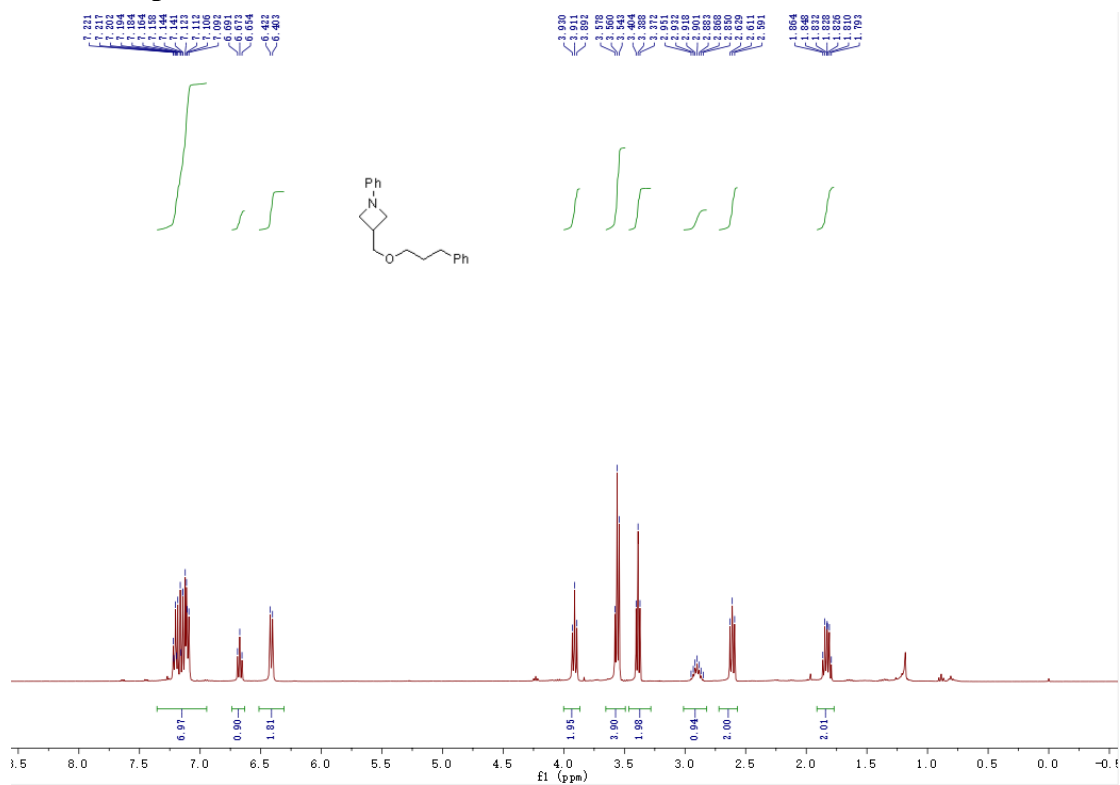
¹H NMR spectrum of 30



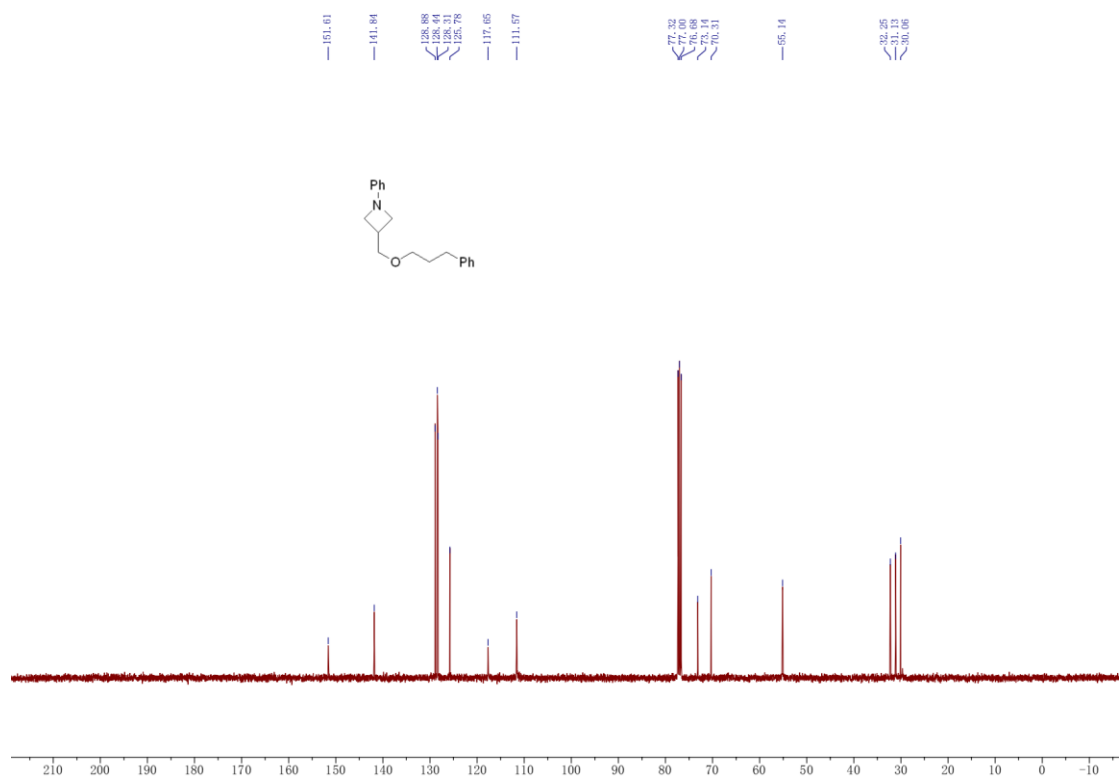
¹³C NMR spectrum of 30



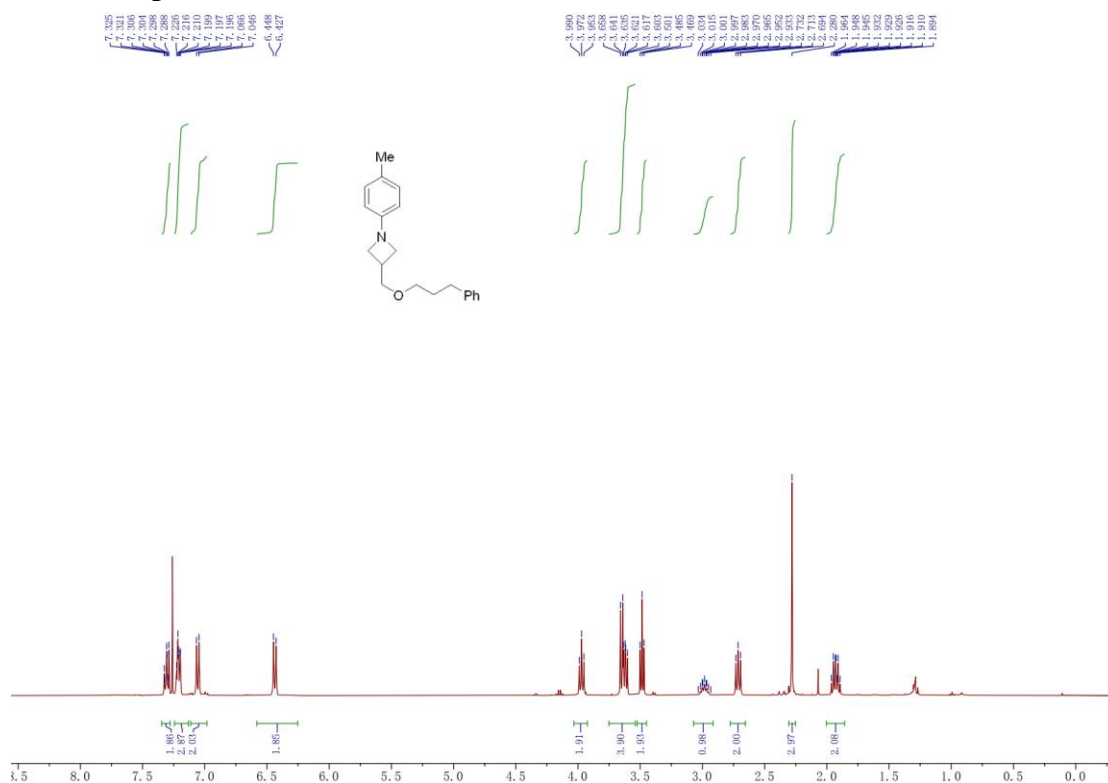
¹H NMR spectrum of 31



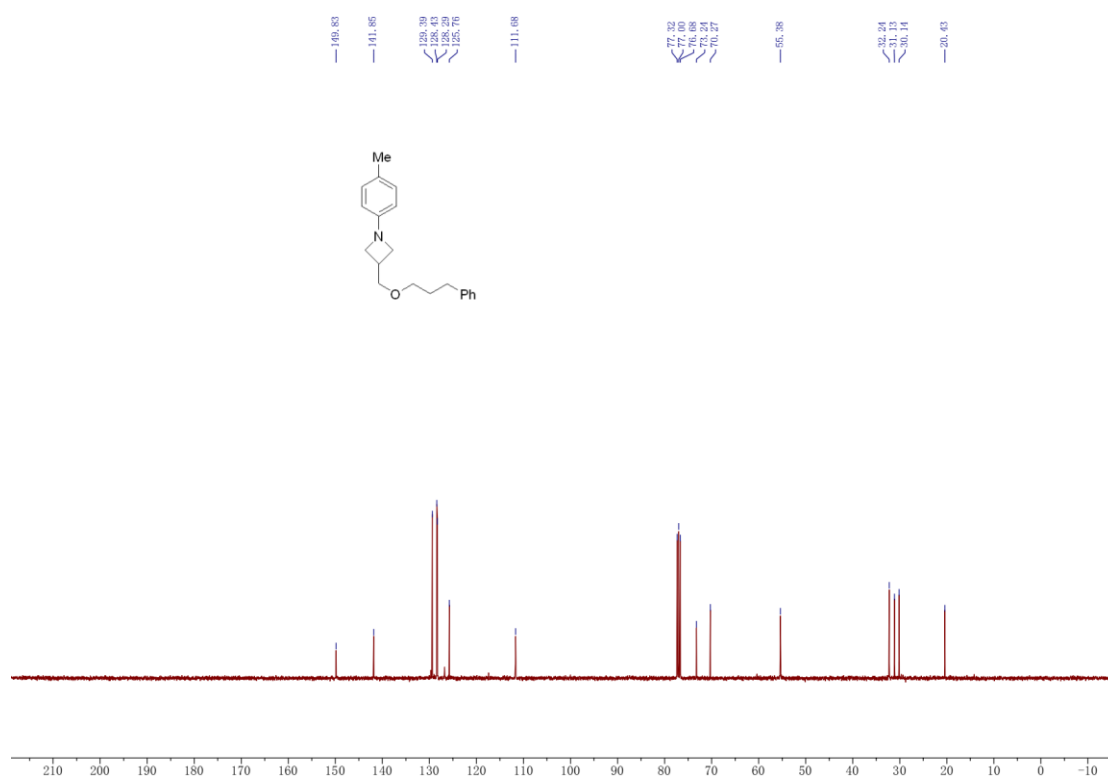
¹³C NMR spectrum of 31



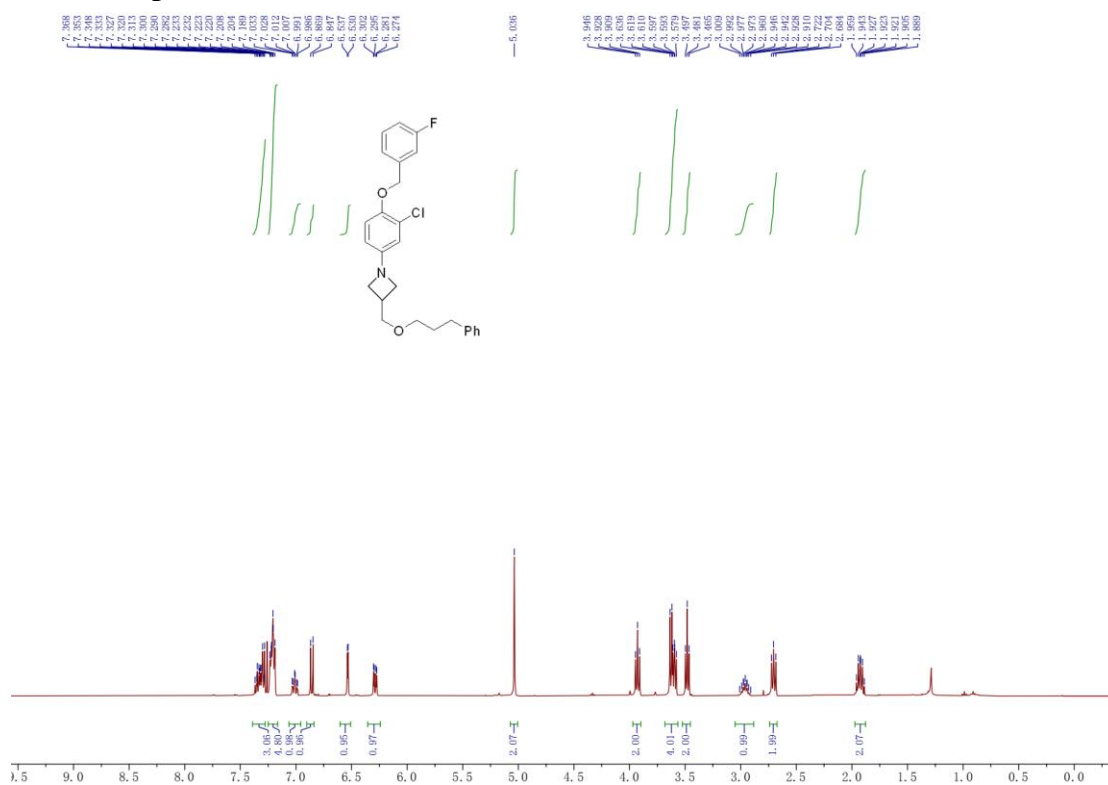
¹H NMR spectrum of 32



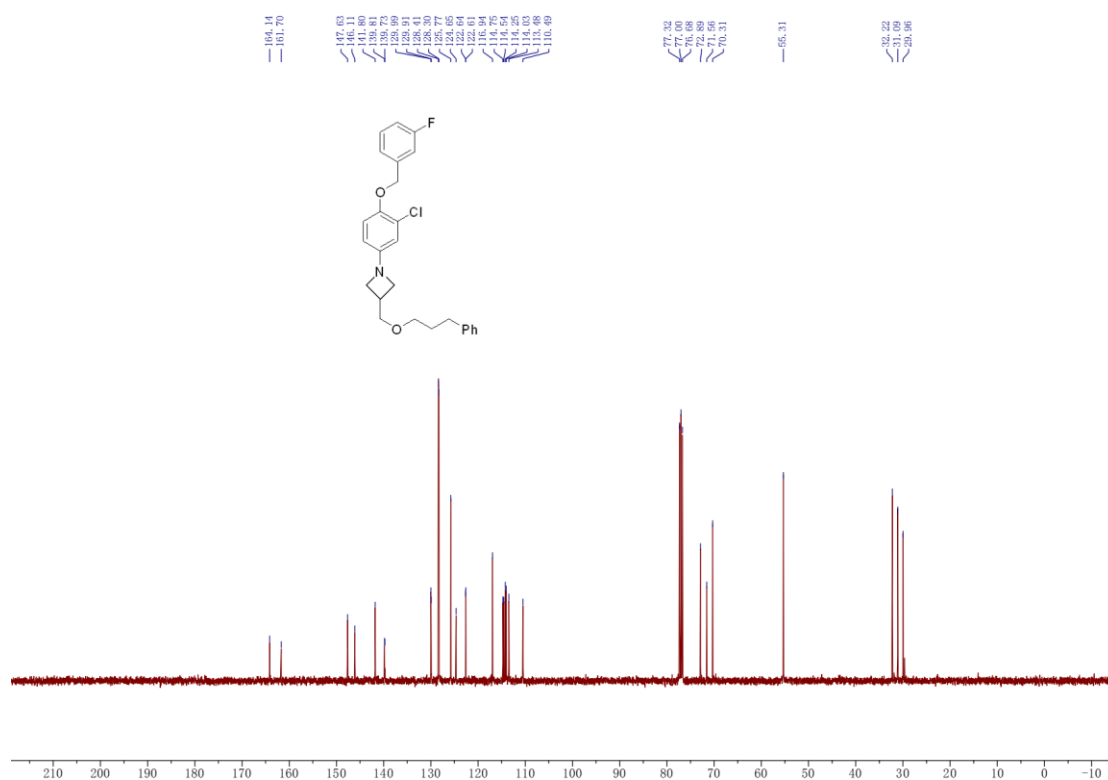
¹³C NMR spectrum of 32



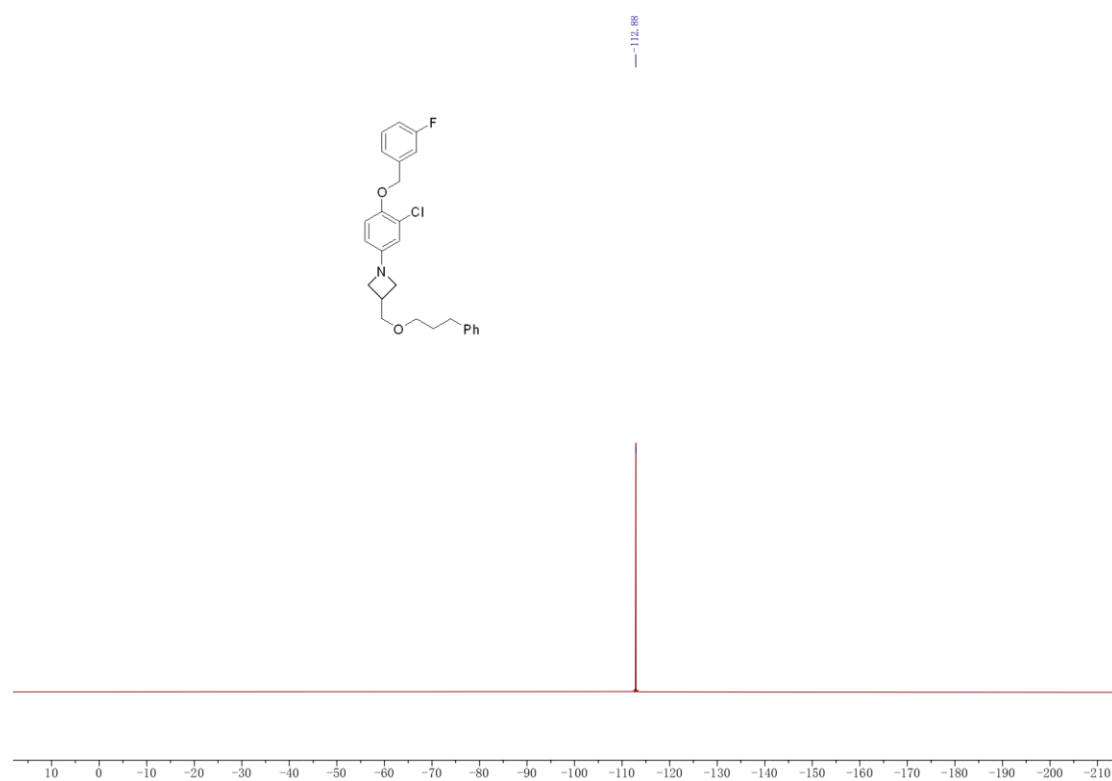
¹H NMR spectrum of 33



¹³C NMR spectrum of 33



¹⁹F NMR spectrum of 33



¹H NMR spectrum (CDCl₃) of 1-(4-phenylphenoxy)-N,N-diphenylpyrrolidine.

Chemical structure: c1ccc(cc1)OCCN(Cc2ccccc2)C3CCCC3

Peak list (ppm): 7.415, 7.411, 7.406, 7.398, 7.394, 7.391, 7.288, 7.283, 7.279, 7.274, 7.268, 7.265, 7.260, 7.256, 7.250, 7.245, 7.243, 7.239, 7.192, 7.188, 7.184, 7.182, 7.179, 7.170, 7.163, 7.159, 7.155, 7.151, 4.370, 3.546, 3.530, 3.500, 3.480, 3.446, 3.398, 3.340, 3.320, 3.302, 2.915, 2.918, 2.901, 2.746, 2.729, 2.712, 2.690, 2.668, 2.652, 2.652, 1.913, 1.897, 1.893, 1.891, 1.881, 1.876, 1.872, 1.865, 1.863, 1.859, 1.843.

Integration values: 3.90, 6.03, 5.03, 1.00, 2.06, 2.05, 1.92, 2.03, 3.08, 2.03.

Chemical structure diagram: c1ccc(cc1)OCCN(Cc2ccccc2)C3CCCC3

Chemical structure: OCCOCc1ccc(cc1)N(Cc2ccccc2)Cc3ccccc3

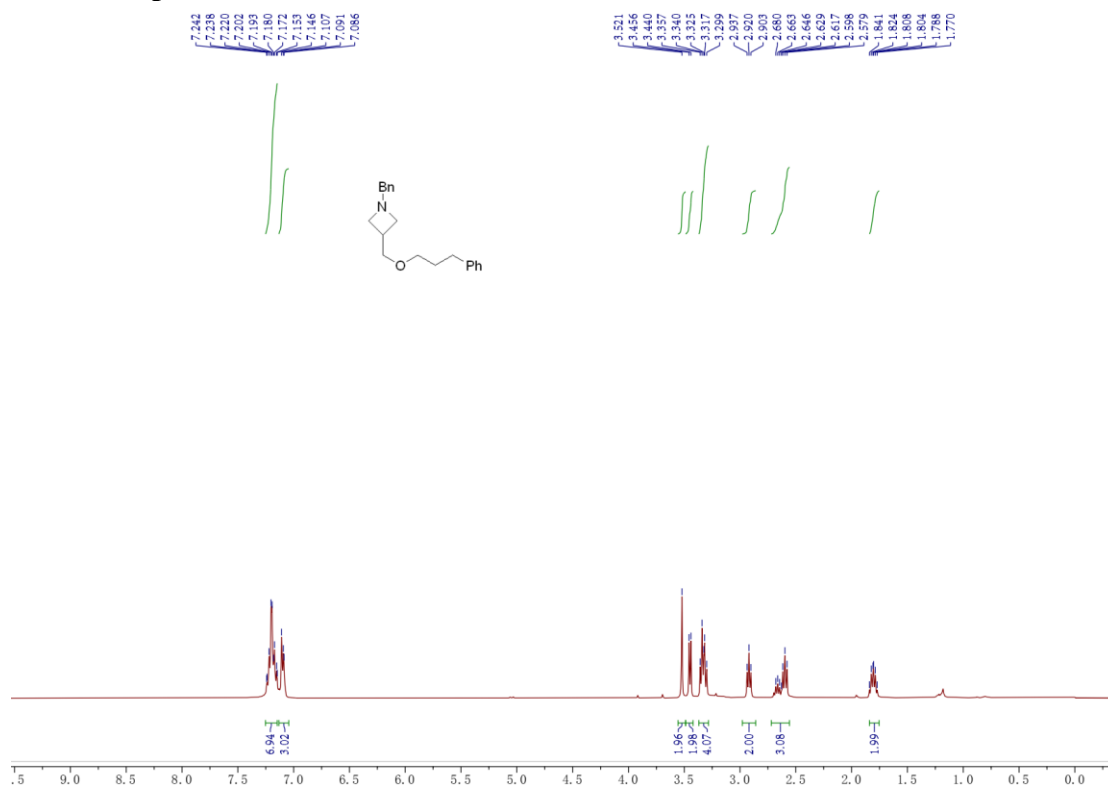
¹³C NMR peaks (ppm):

- 143.07
- 141.91
- 138.43
- 138.38
- 138.35
- 137.51
- 137.03
- 135.14
- 77.95
- 77.92
- 77.60
- 76.08
- 75.21
- 70.07
- 56.56
- 31.28
- 31.23
- 29.77

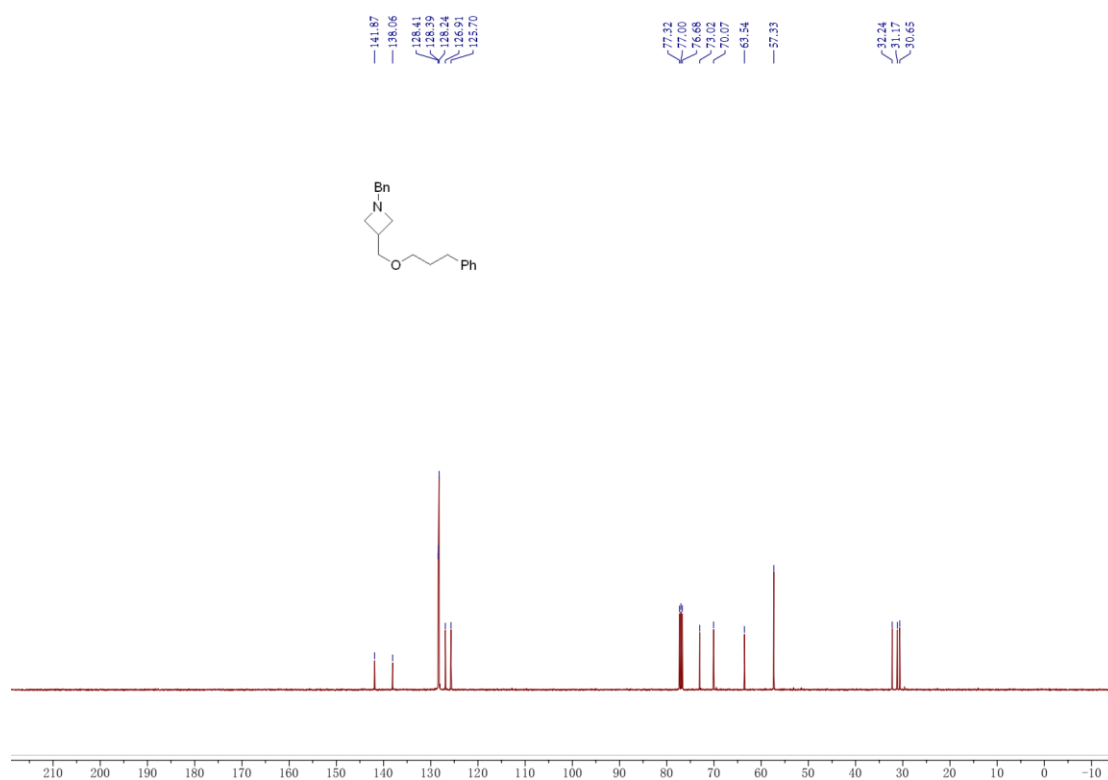
Inset peaks (ppm):

- 142.07
- 141.51

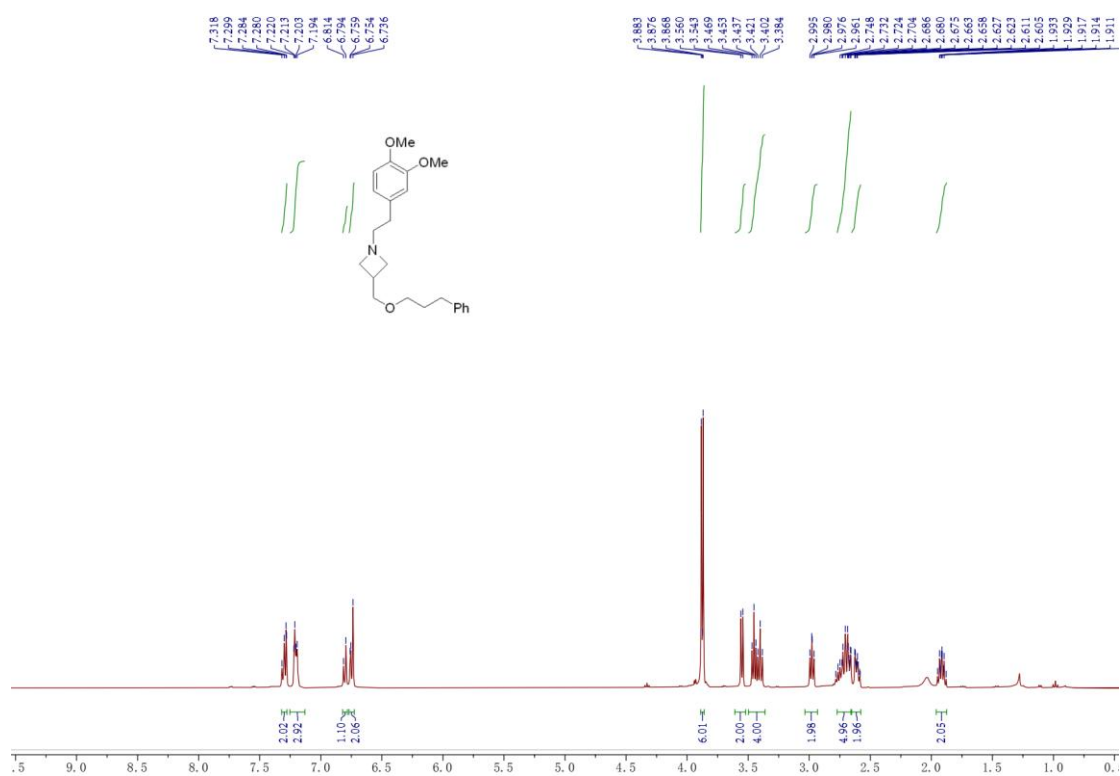
¹H NMR spectrum of 35



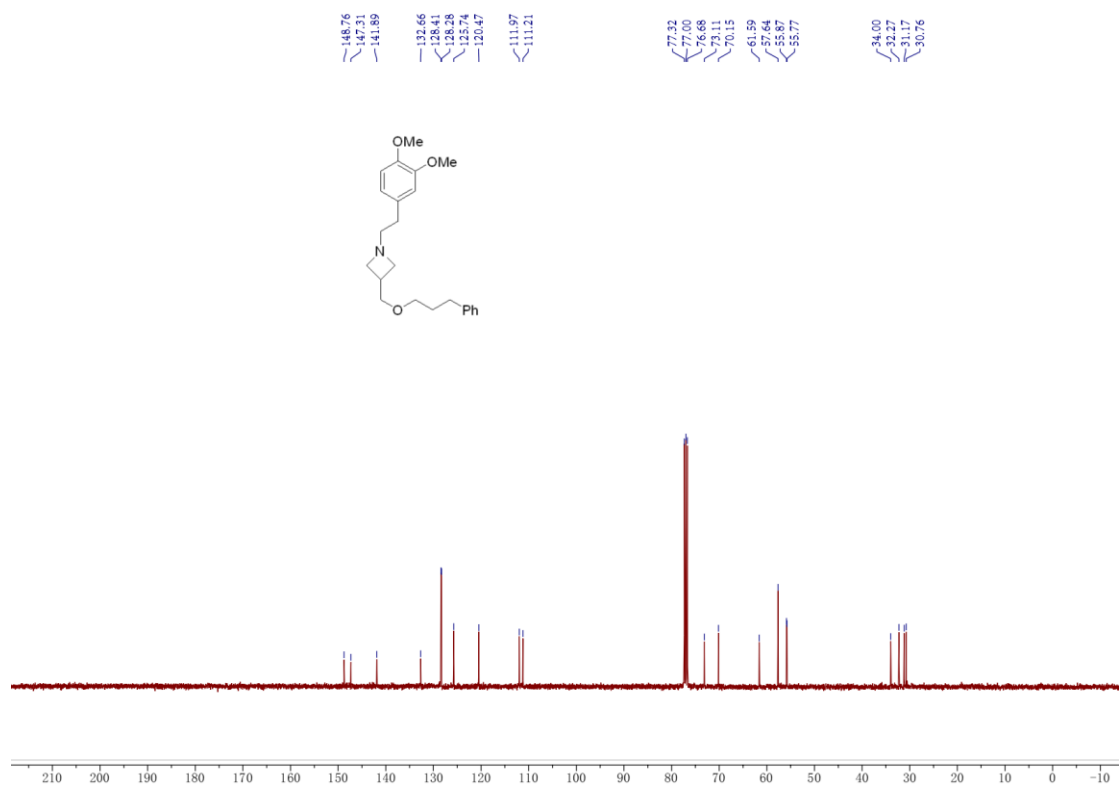
¹³C NMR spectrum of 35



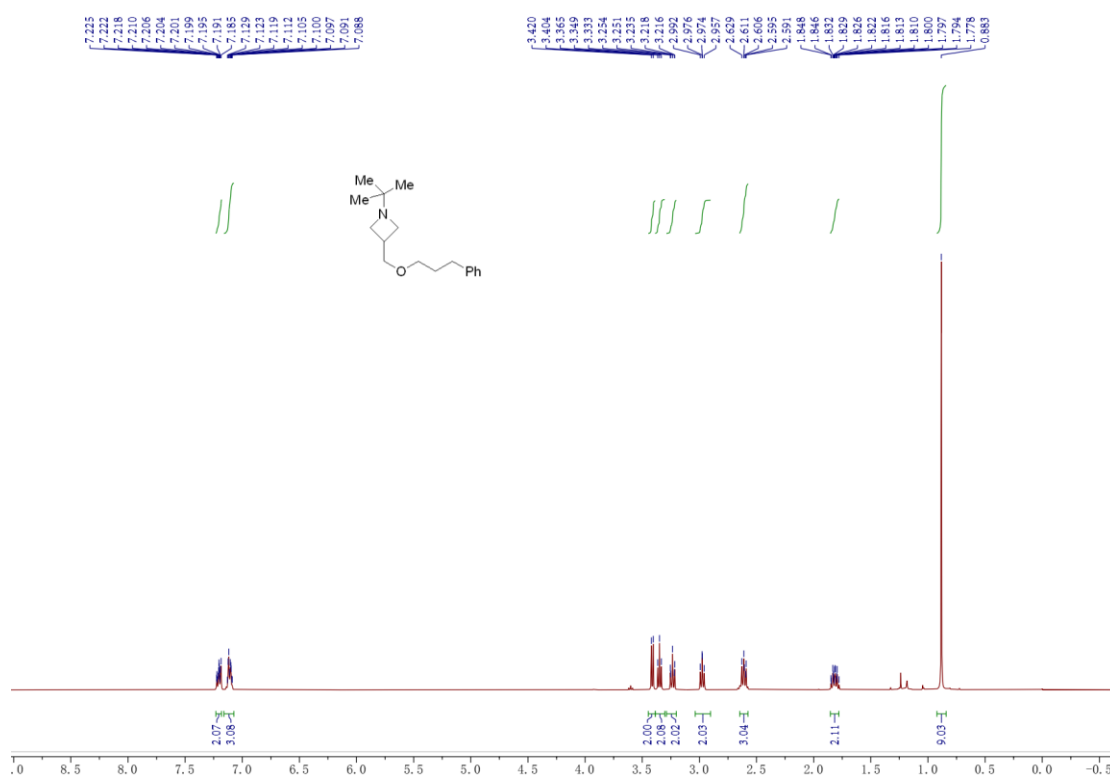
¹H NMR spectrum of 36



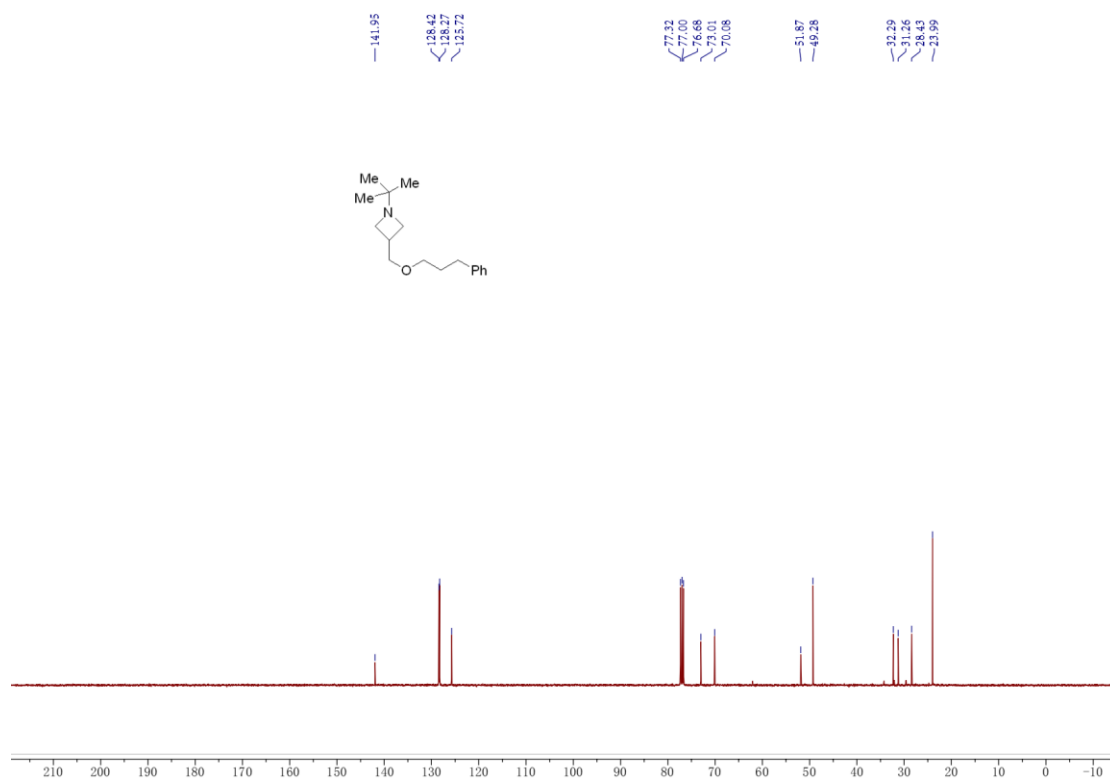
¹³C NMR spectrum of 36



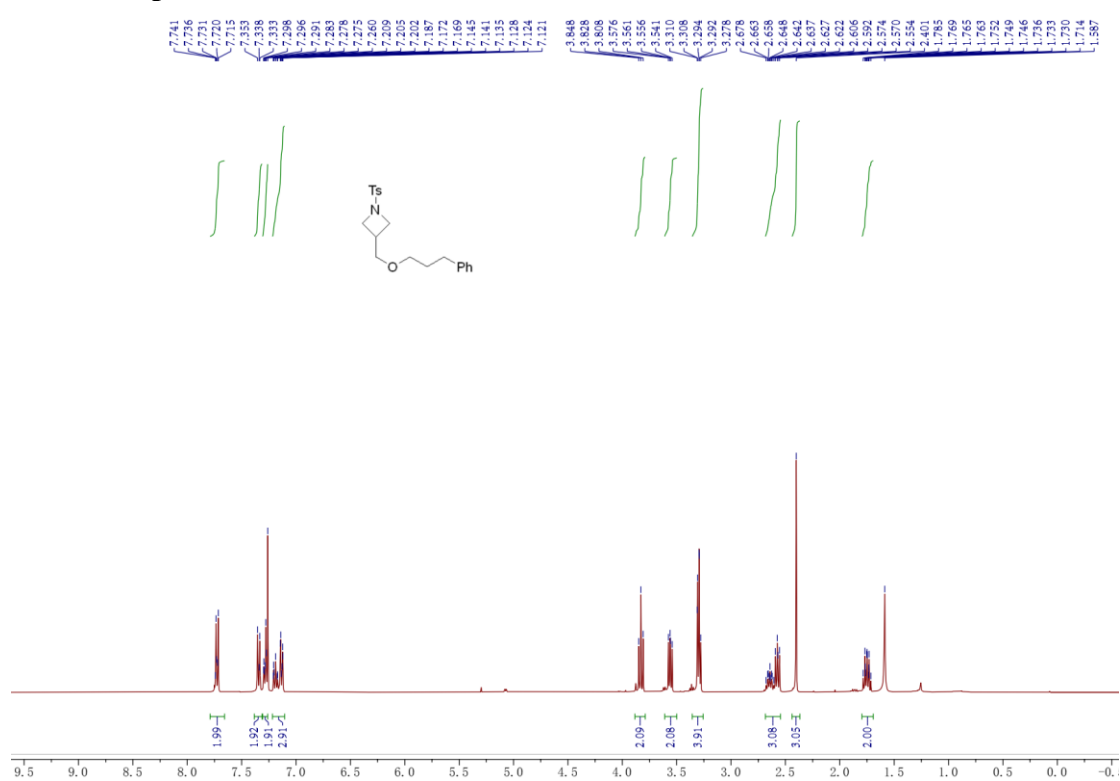
¹H NMR spectrum of 37



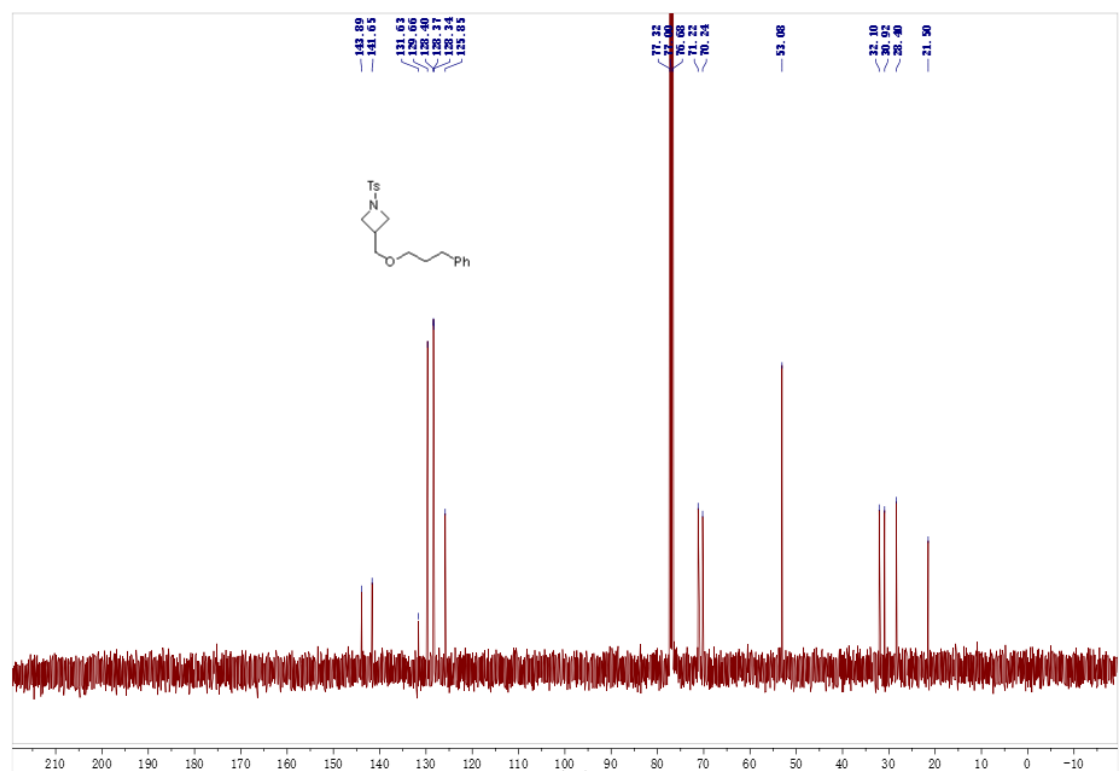
¹³C NMR spectrum of 37



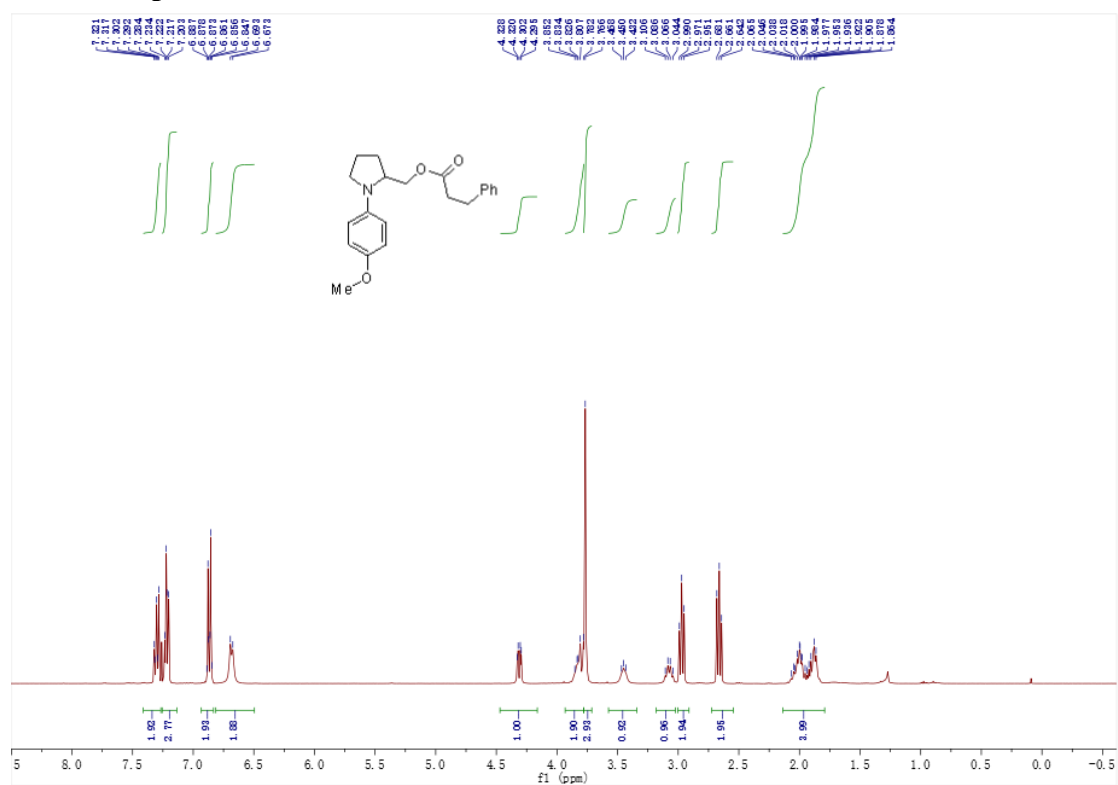
¹H NMR spectrum of 38



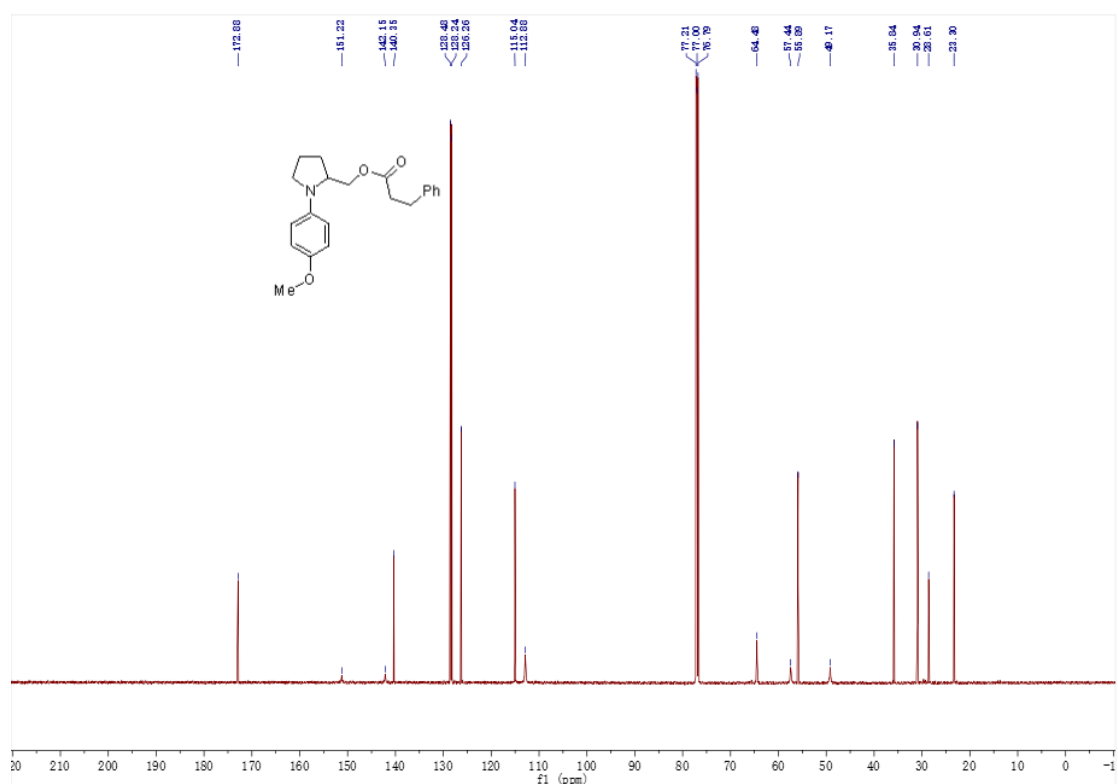
¹³C NMR spectrum of 38



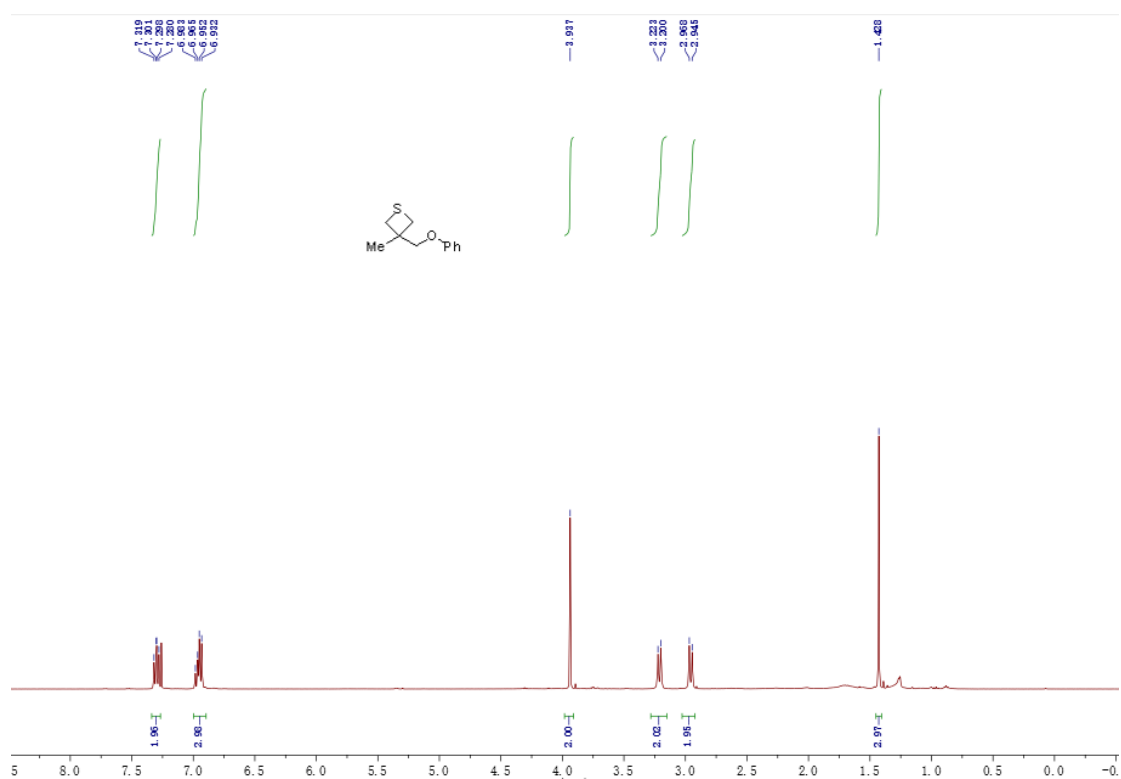
¹H NMR spectrum of 40



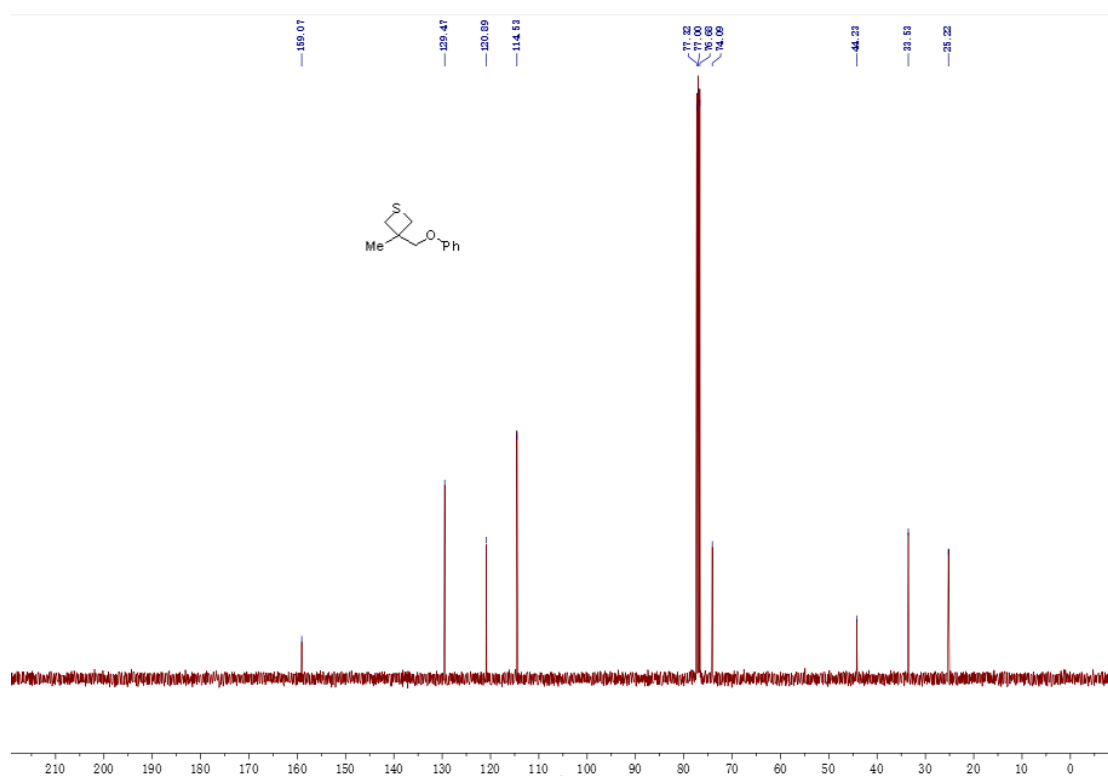
^{13}C NMR spectrum of 40



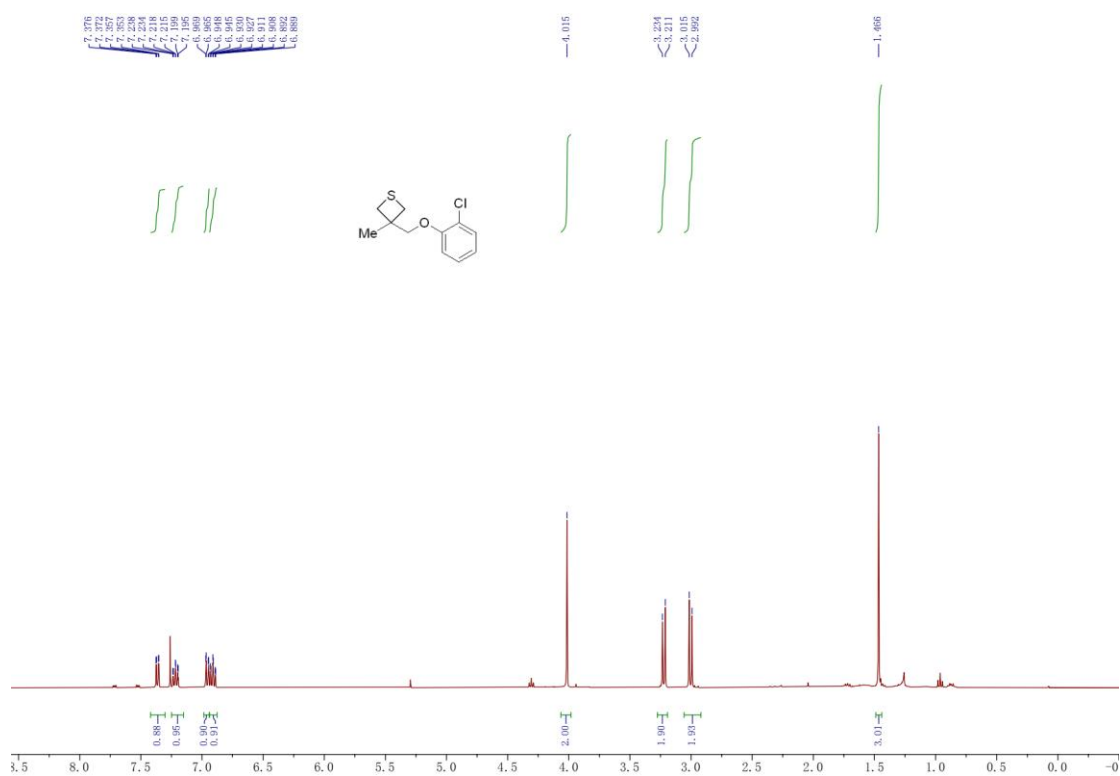
¹H NMR spectrum of 43



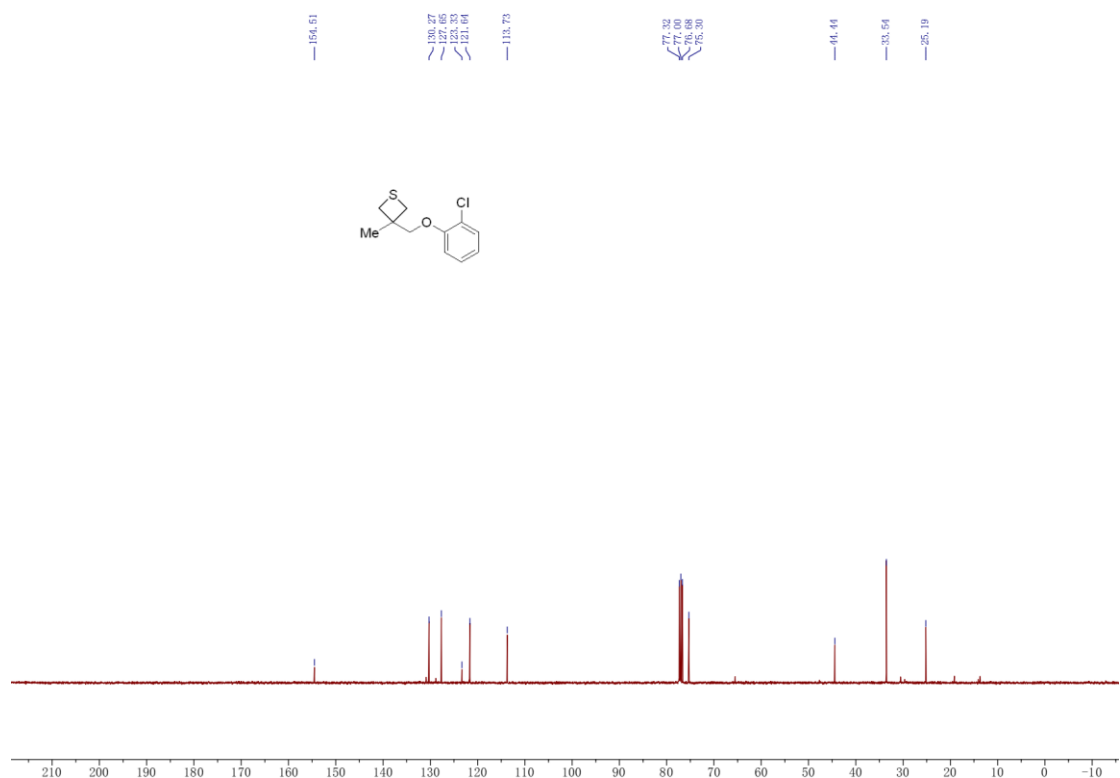
¹³C NMR spectrum of 43



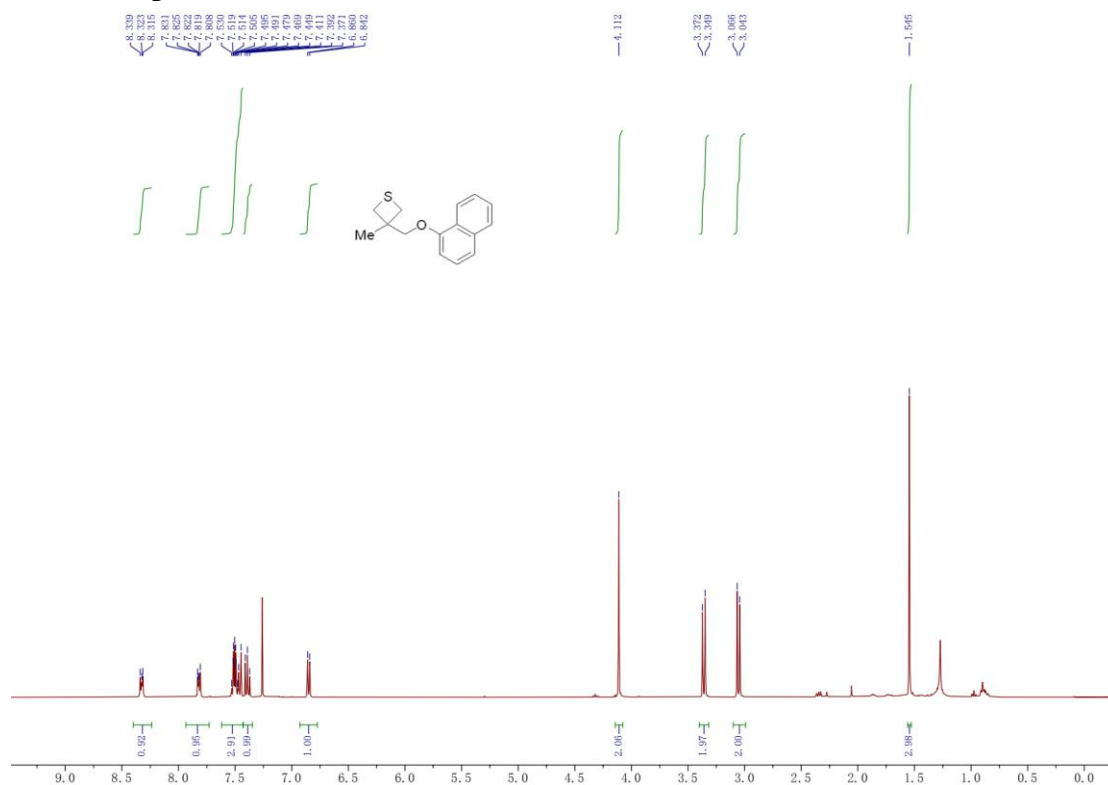
¹H NMR spectrum of 44



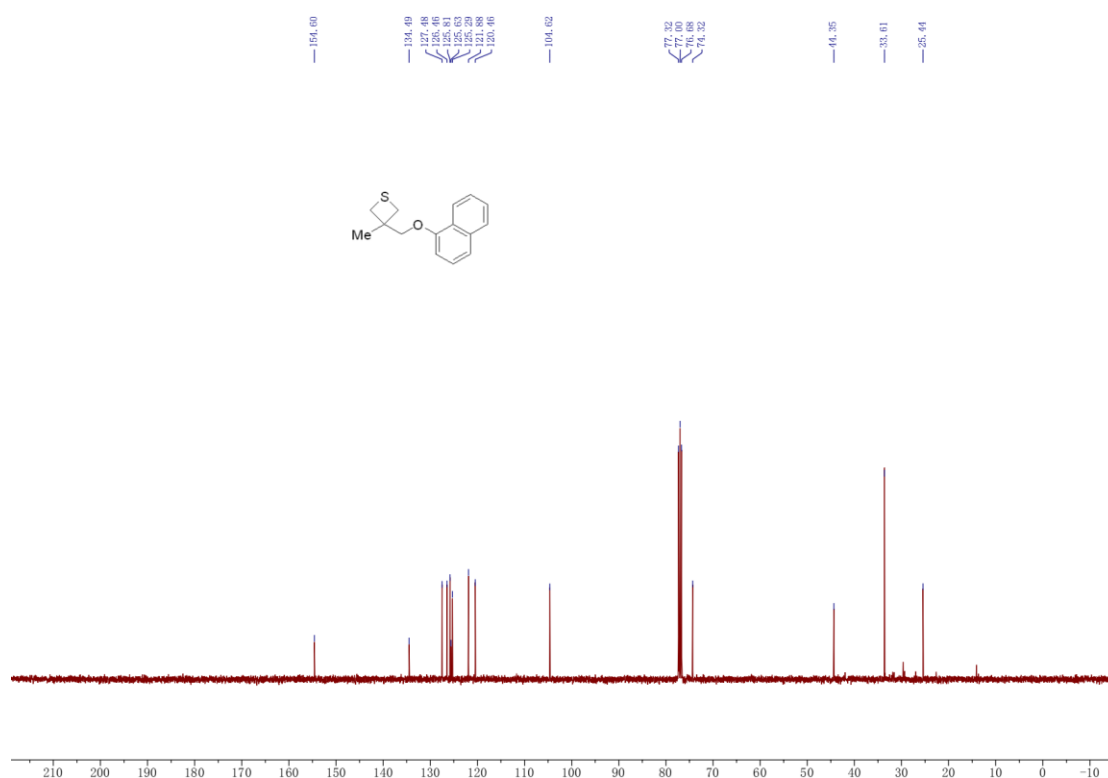
¹³C NMR spectrum of 44



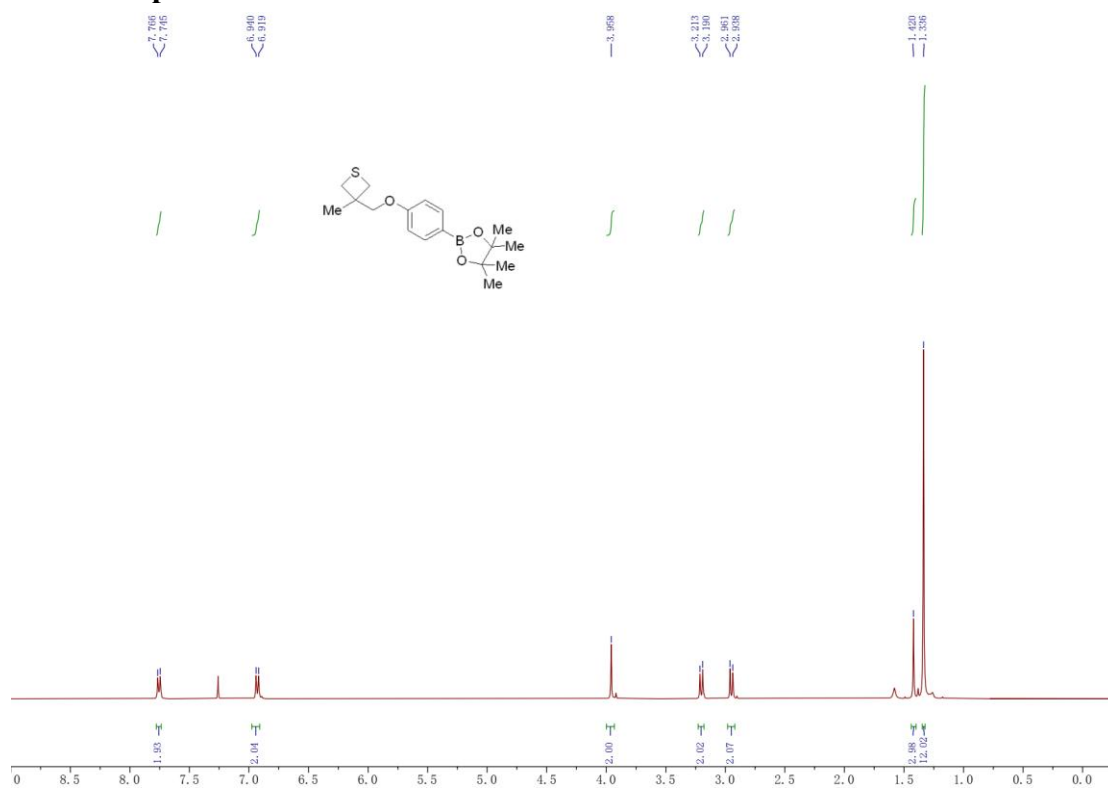
¹H NMR spectrum of 45



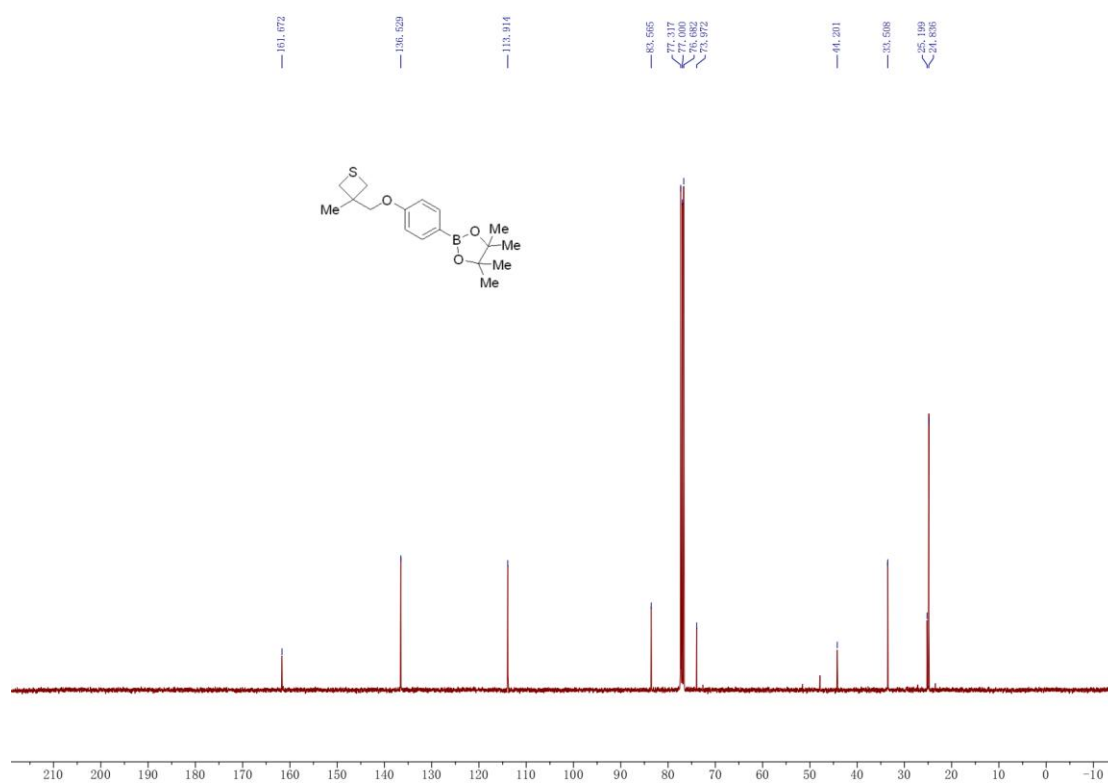
¹³C NMR spectrum of 45



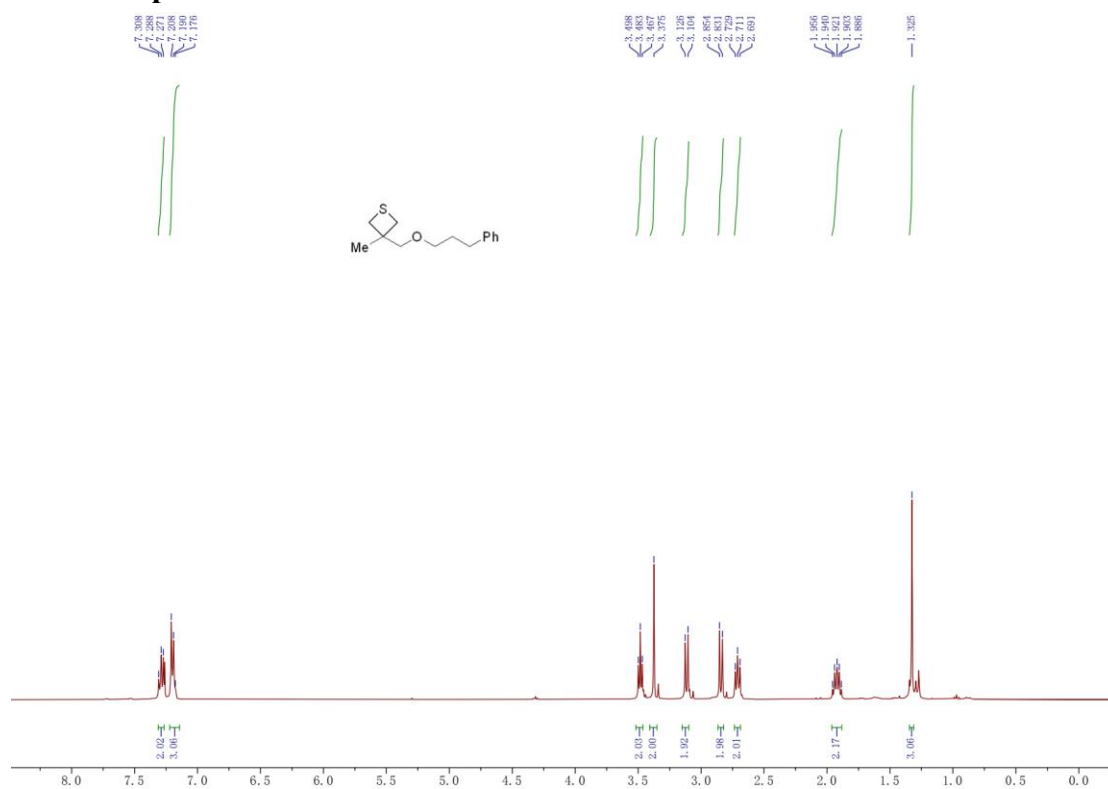
¹H NMR spectrum of 46



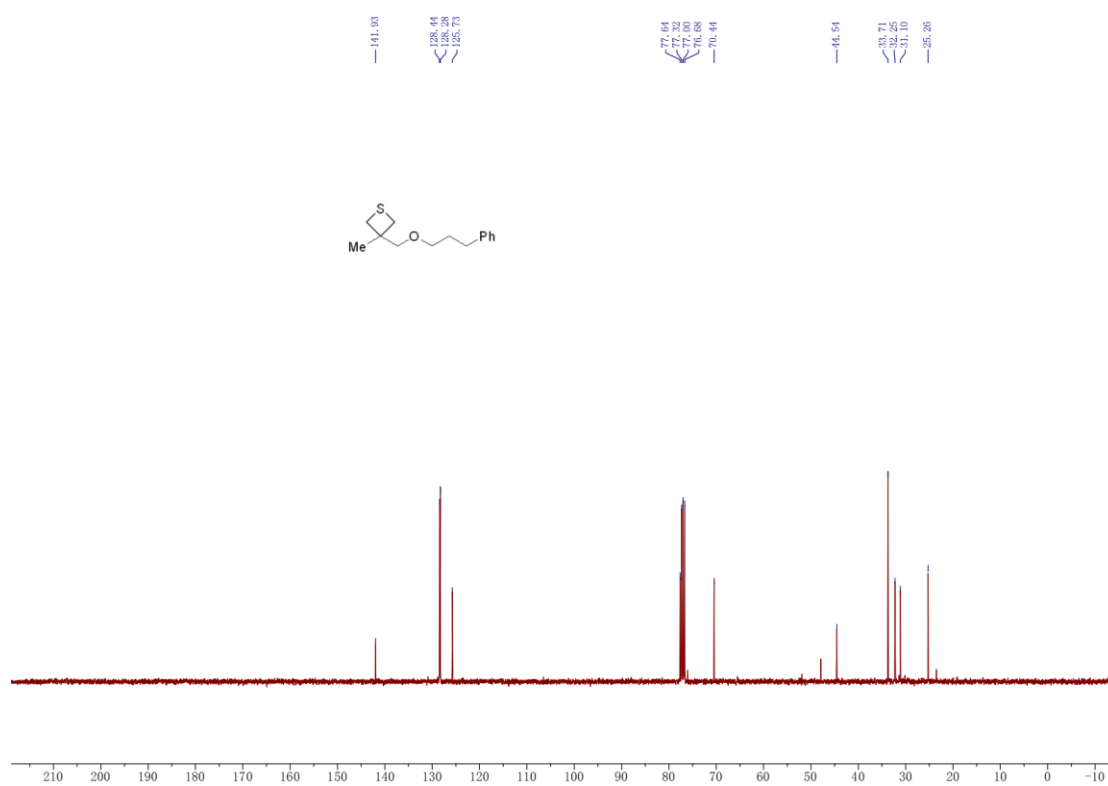
¹³C NMR spectrum of 46



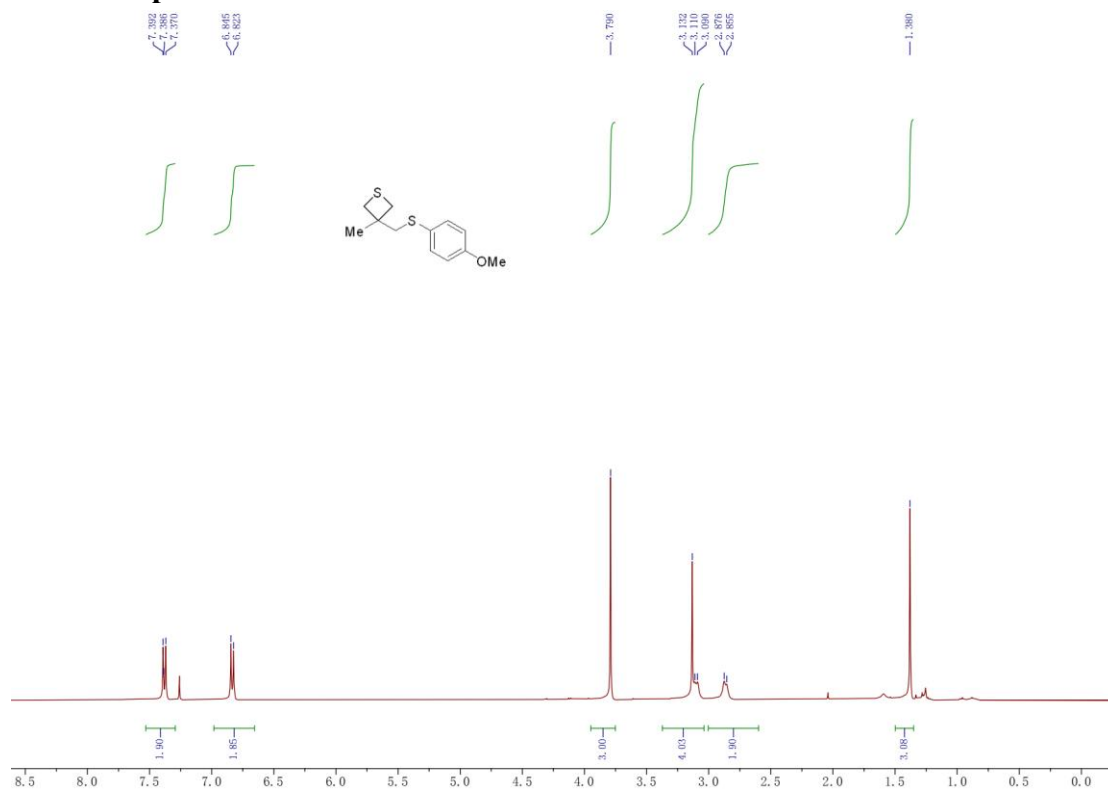
¹H NMR spectrum of 47



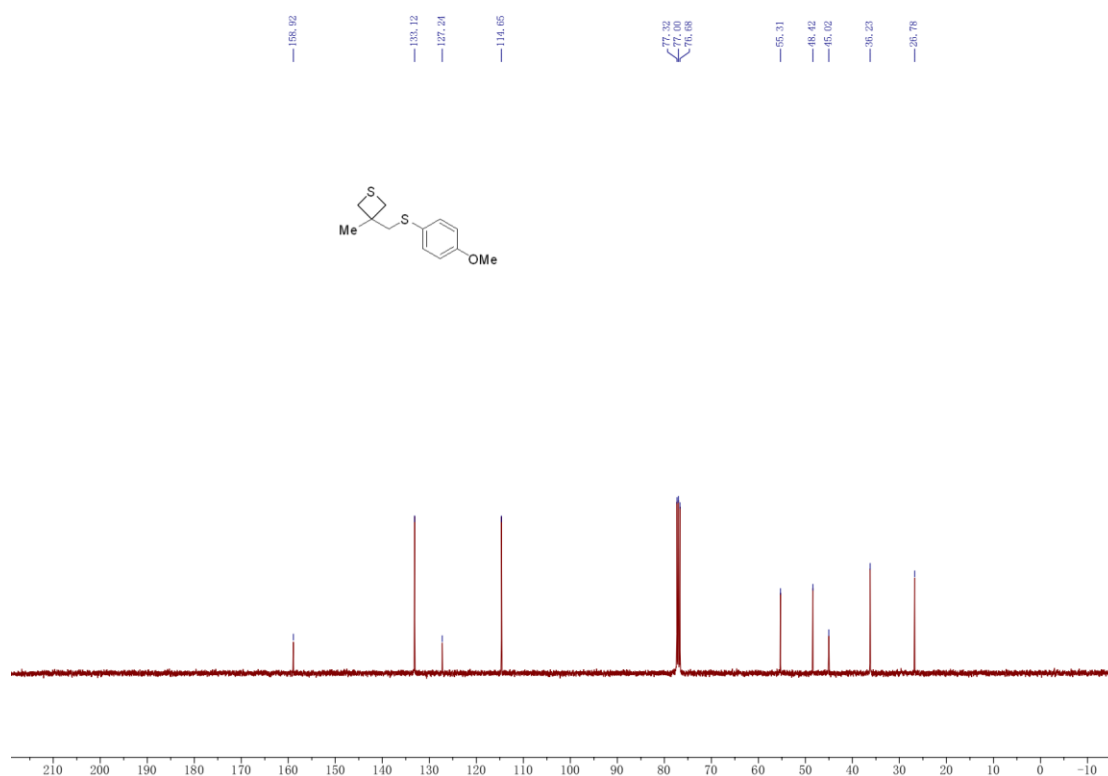
¹³C NMR spectrum of 47



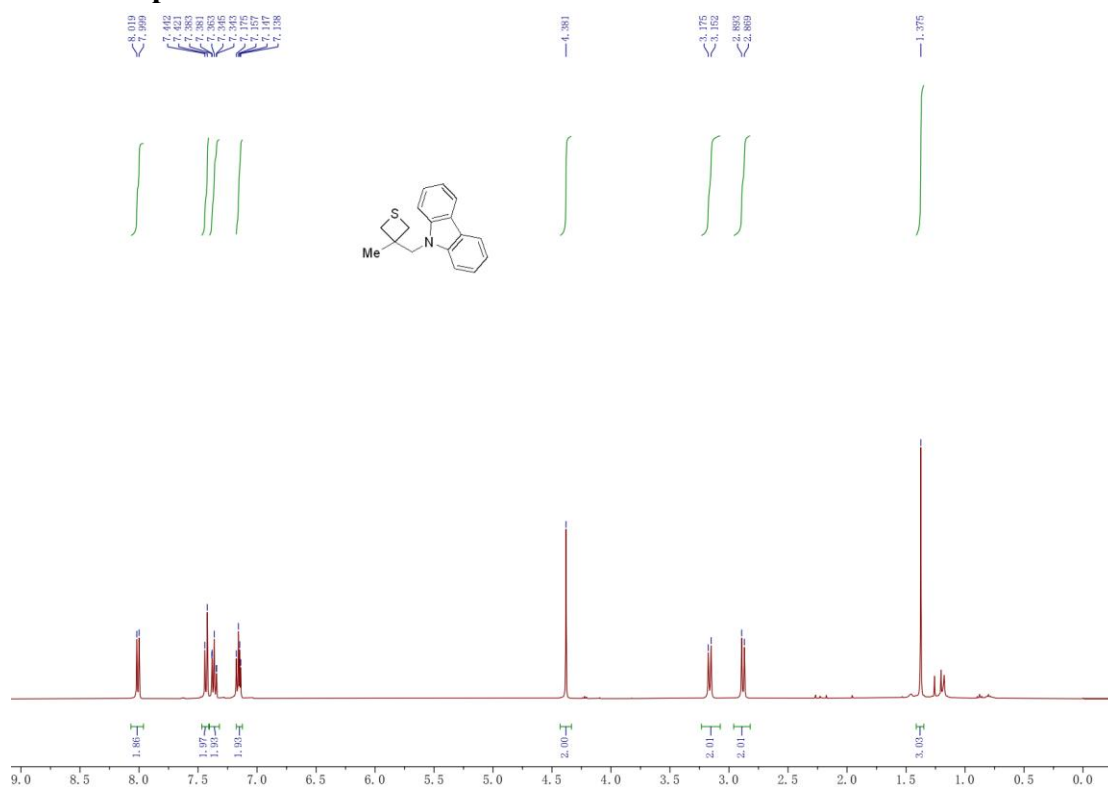
¹H NMR spectrum of 48



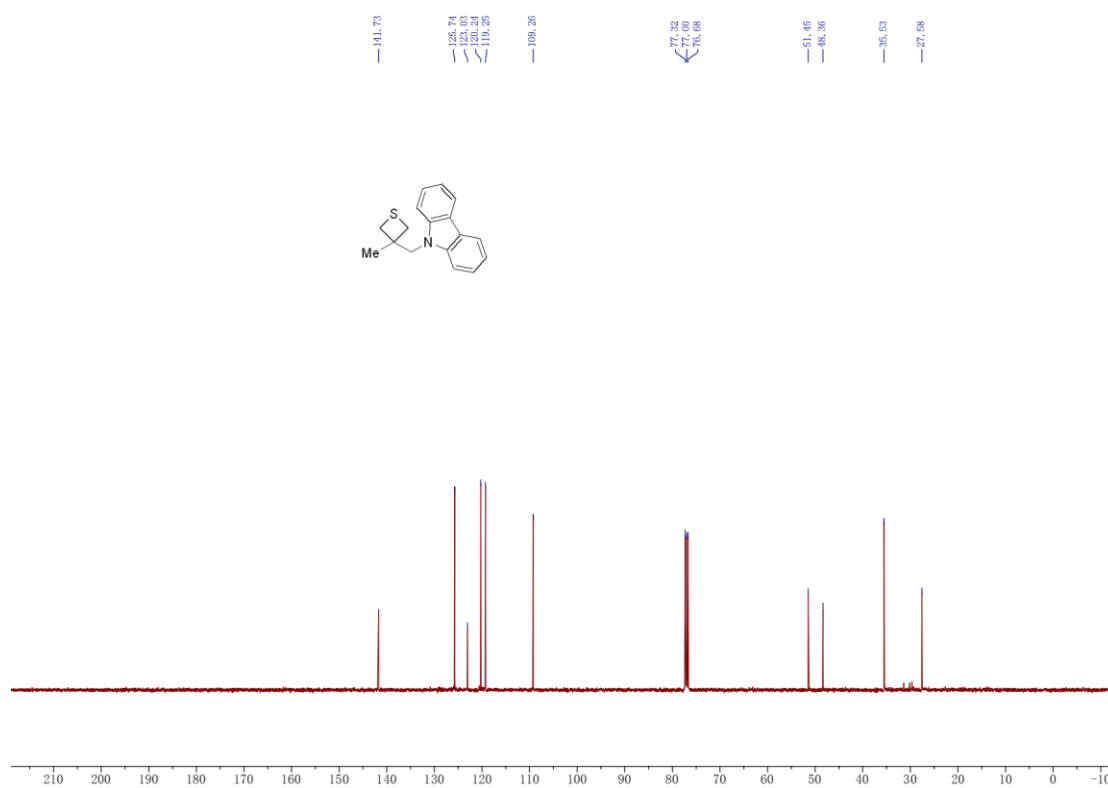
¹³C NMR spectrum of 48



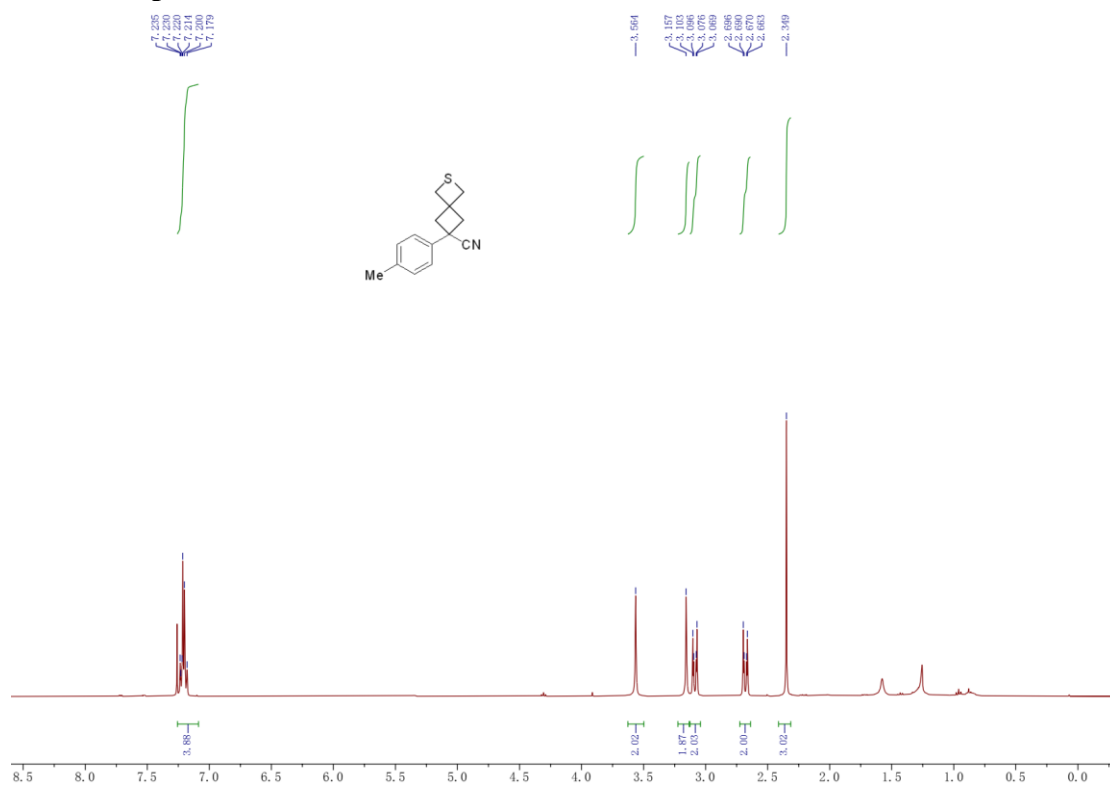
¹H NMR spectrum of 49



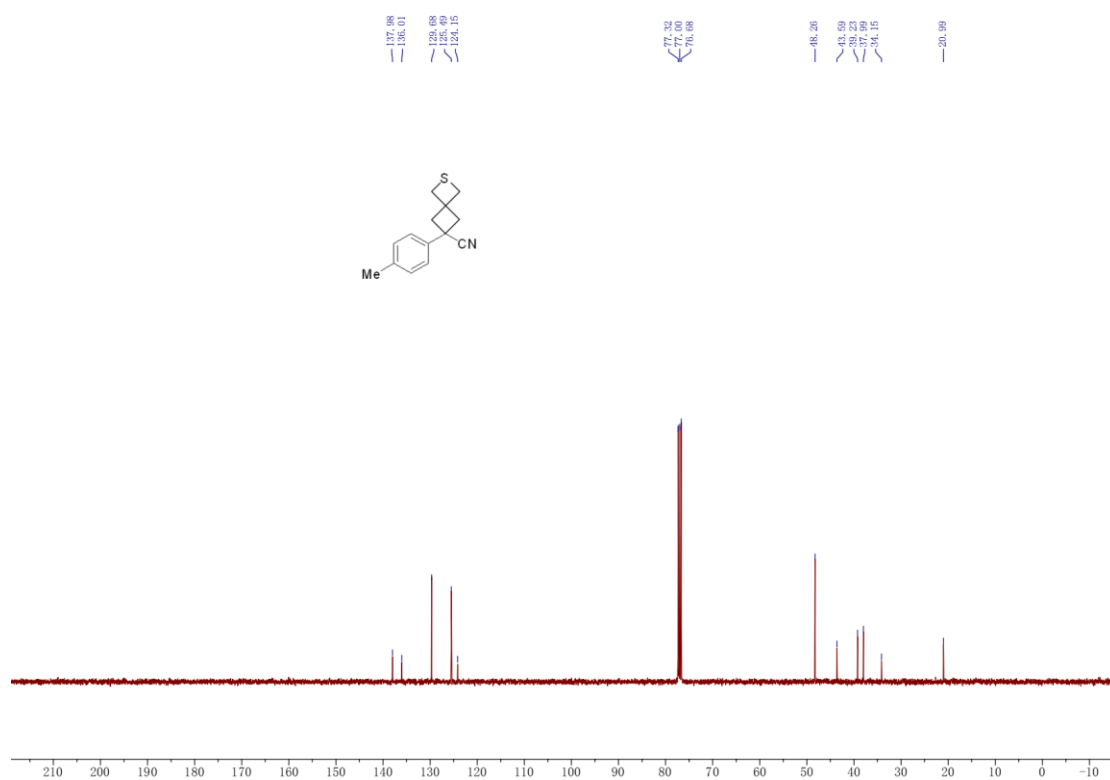
¹³C NMR spectrum of 49



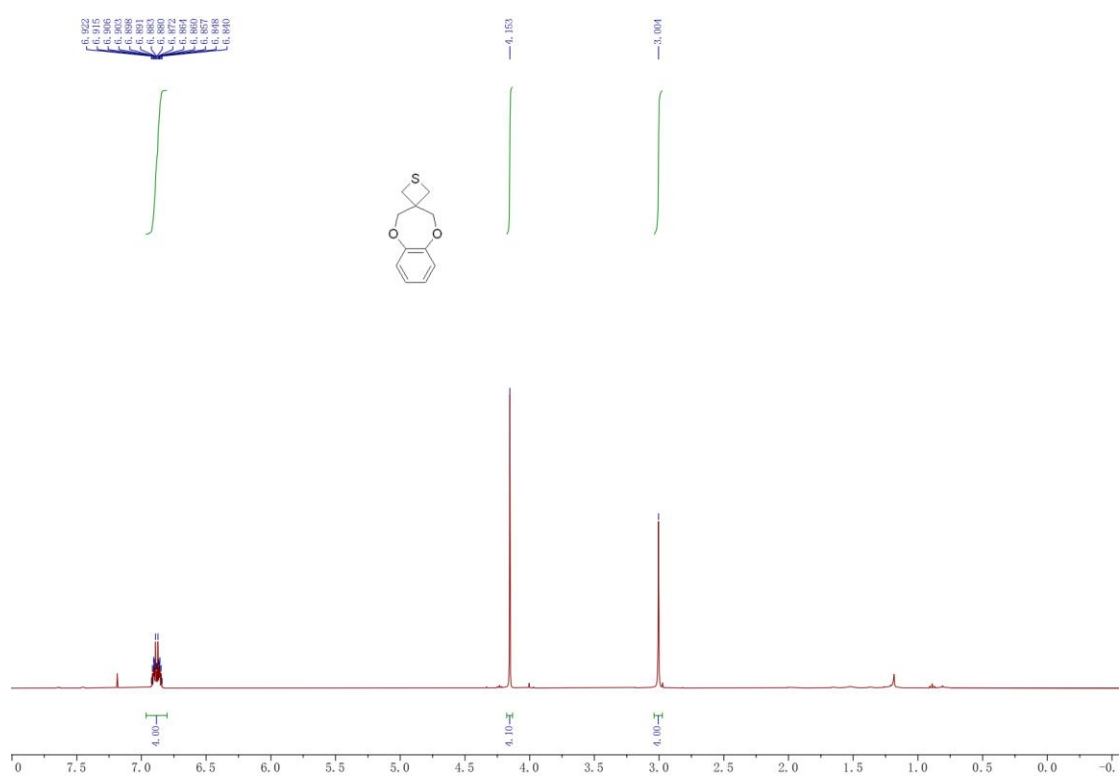
¹H NMR spectrum of 50



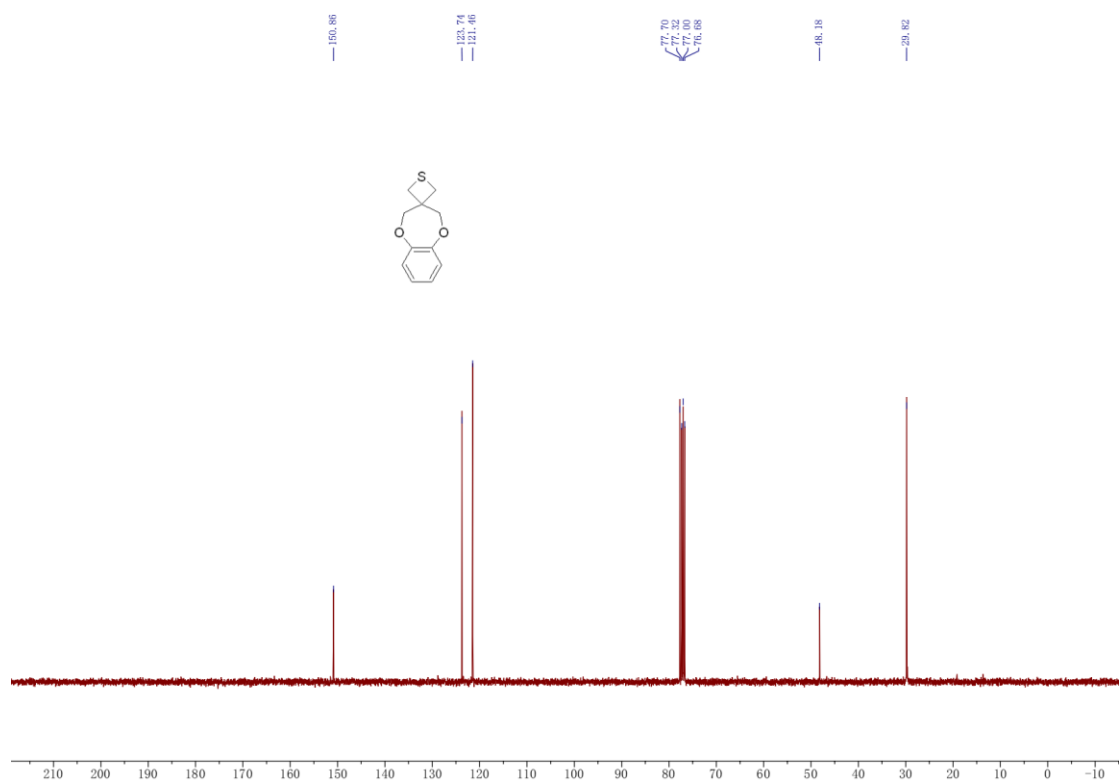
¹³C NMR spectrum of 50



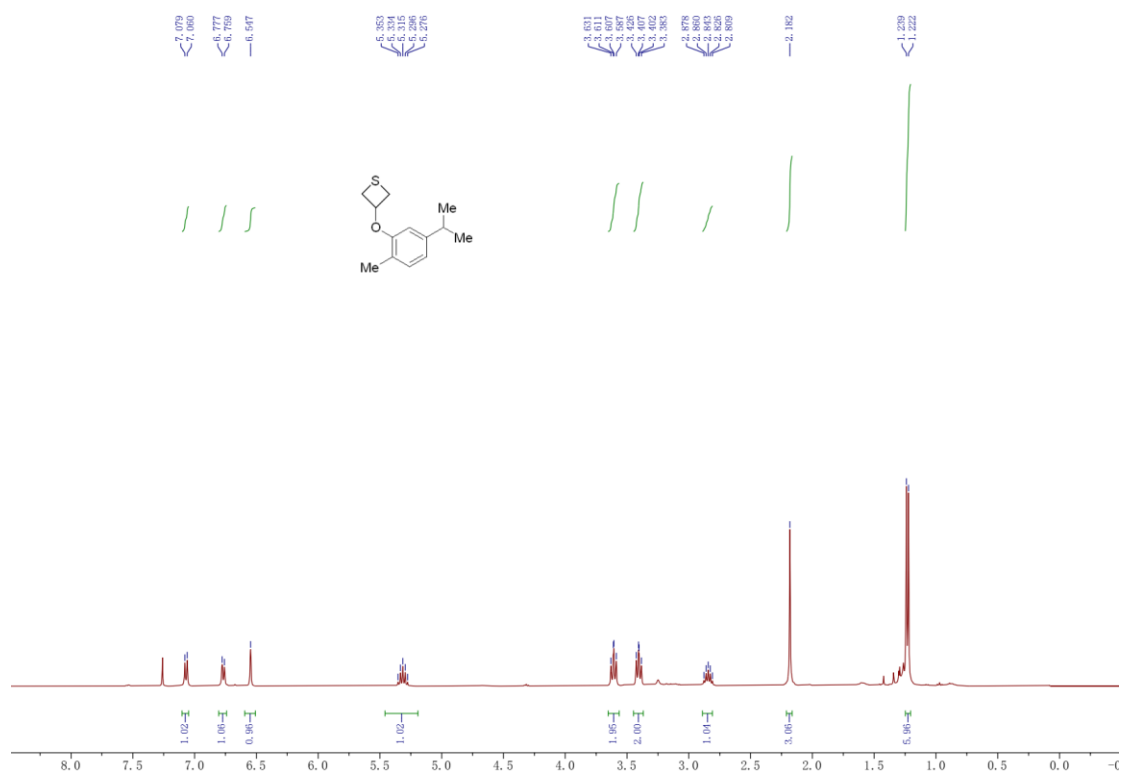
¹H NMR spectrum of 51



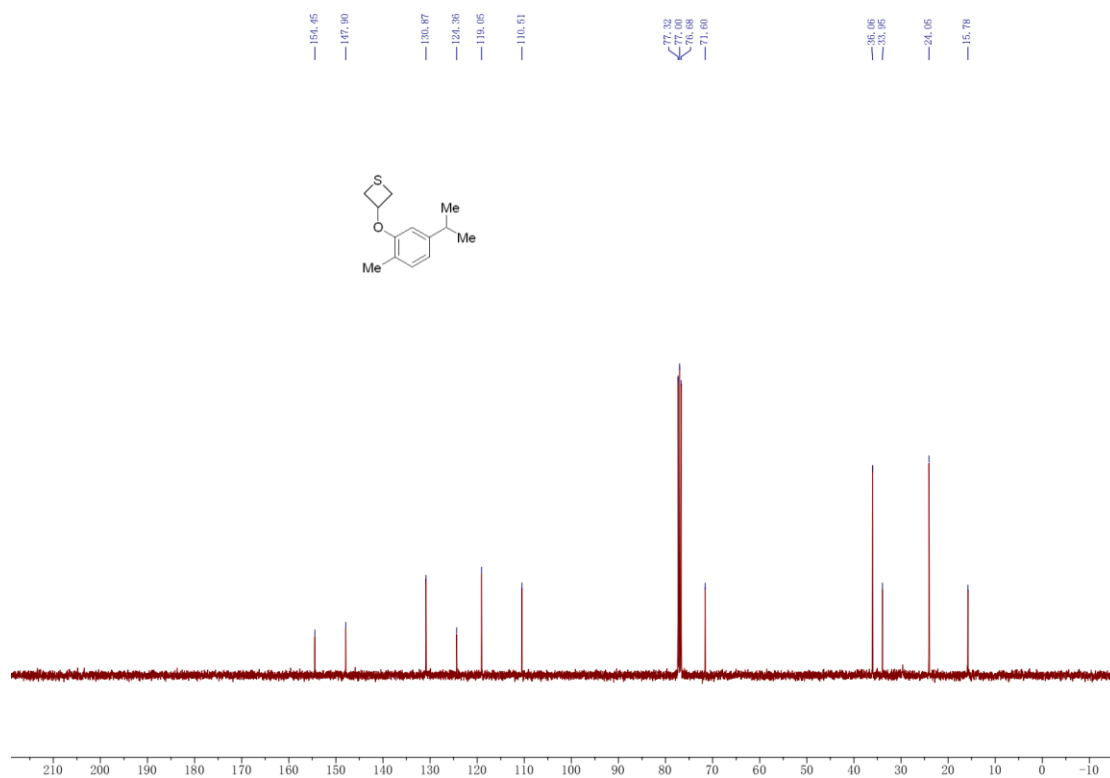
¹³C NMR spectrum of 51



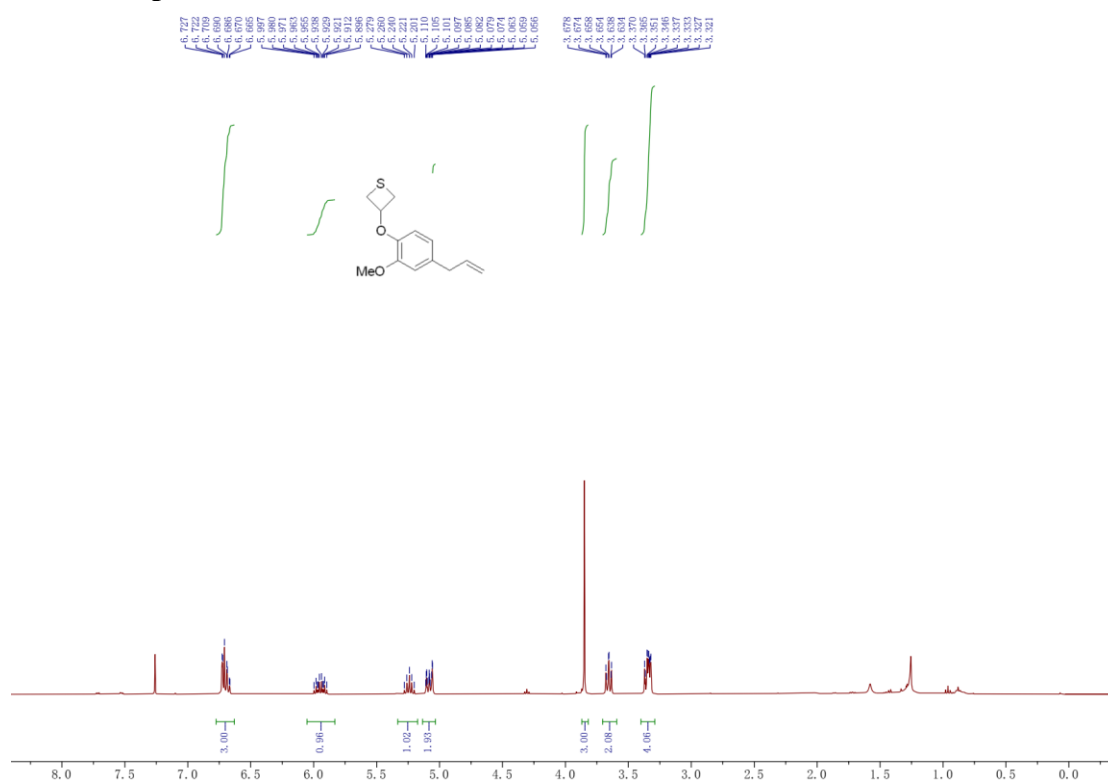
¹H NMR spectrum of 52



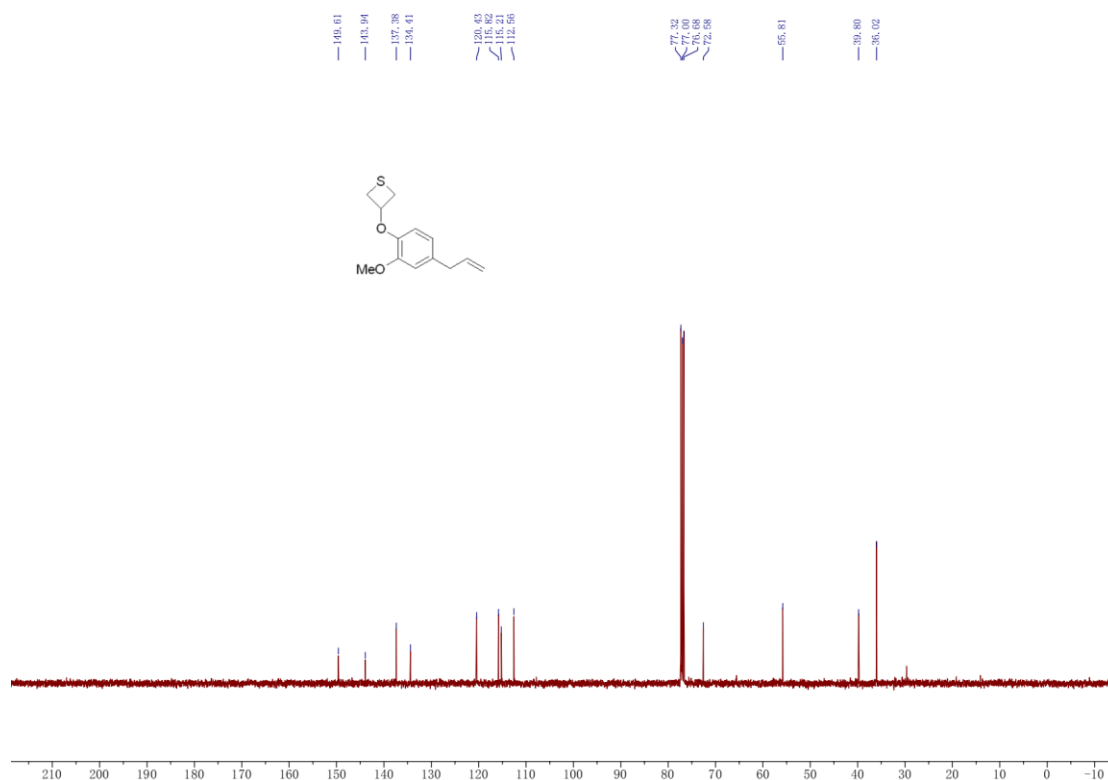
¹³C NMR spectrum of 52



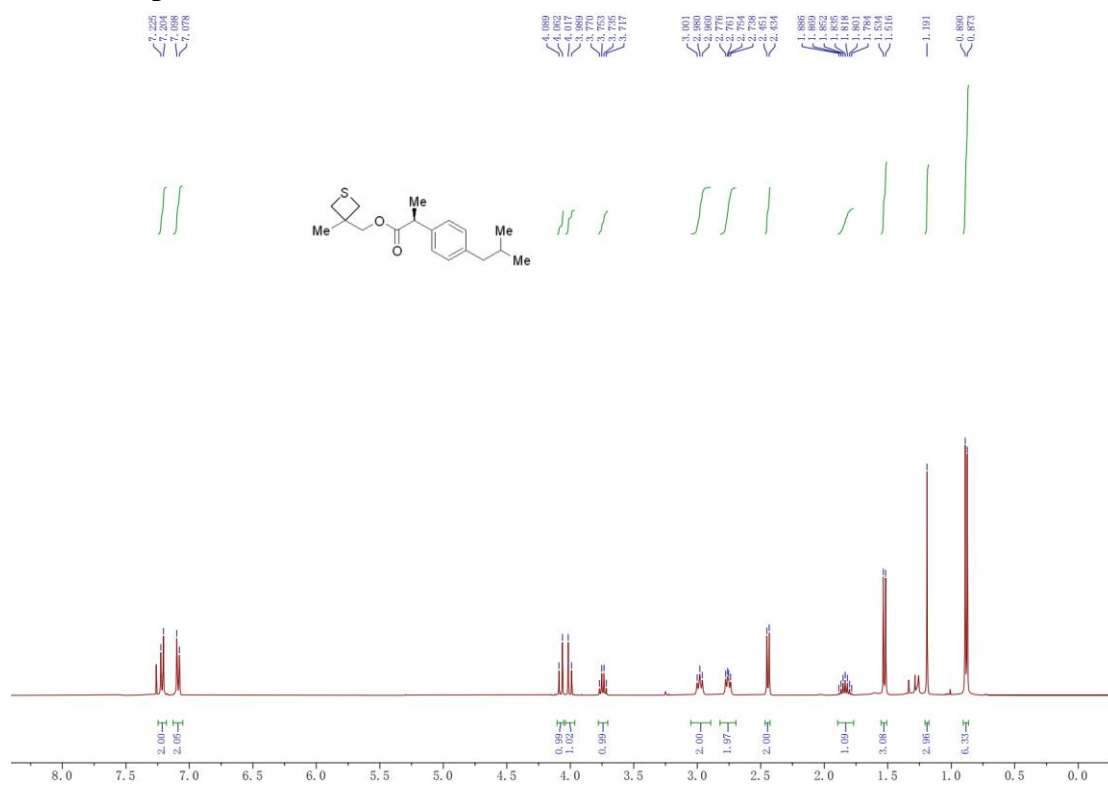
¹H NMR spectrum of 53



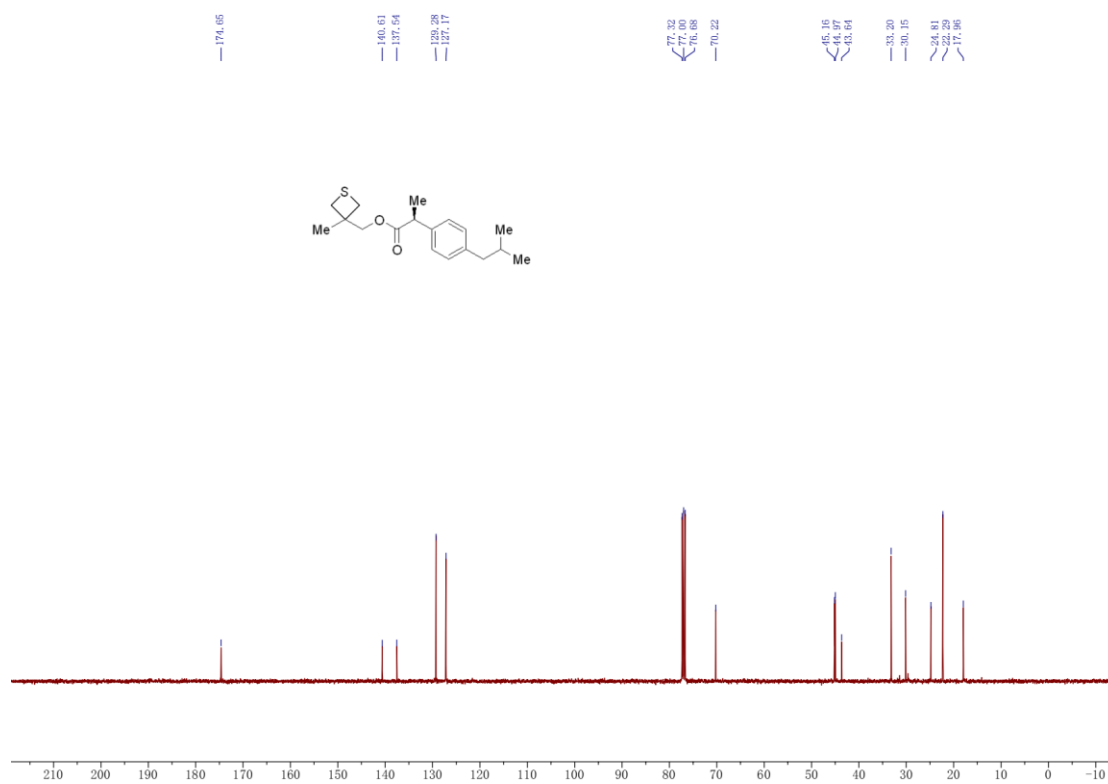
¹³C NMR spectrum of 53



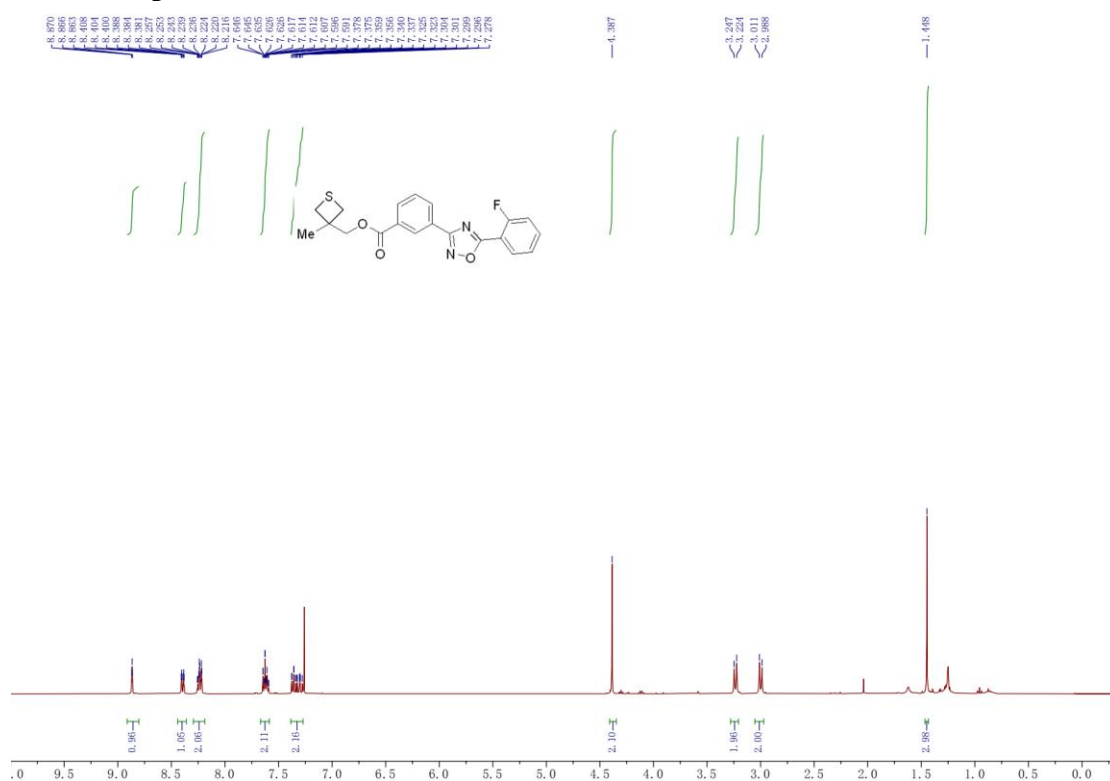
¹H NMR spectrum of 54



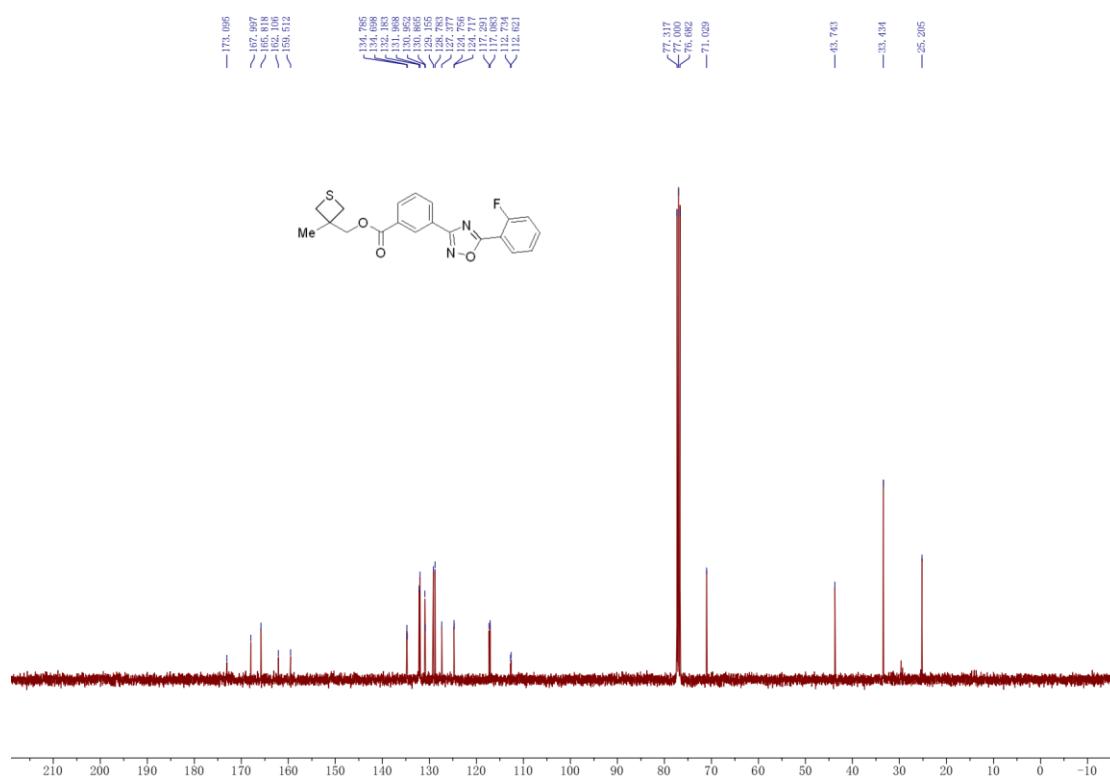
¹³C NMR spectrum of 54



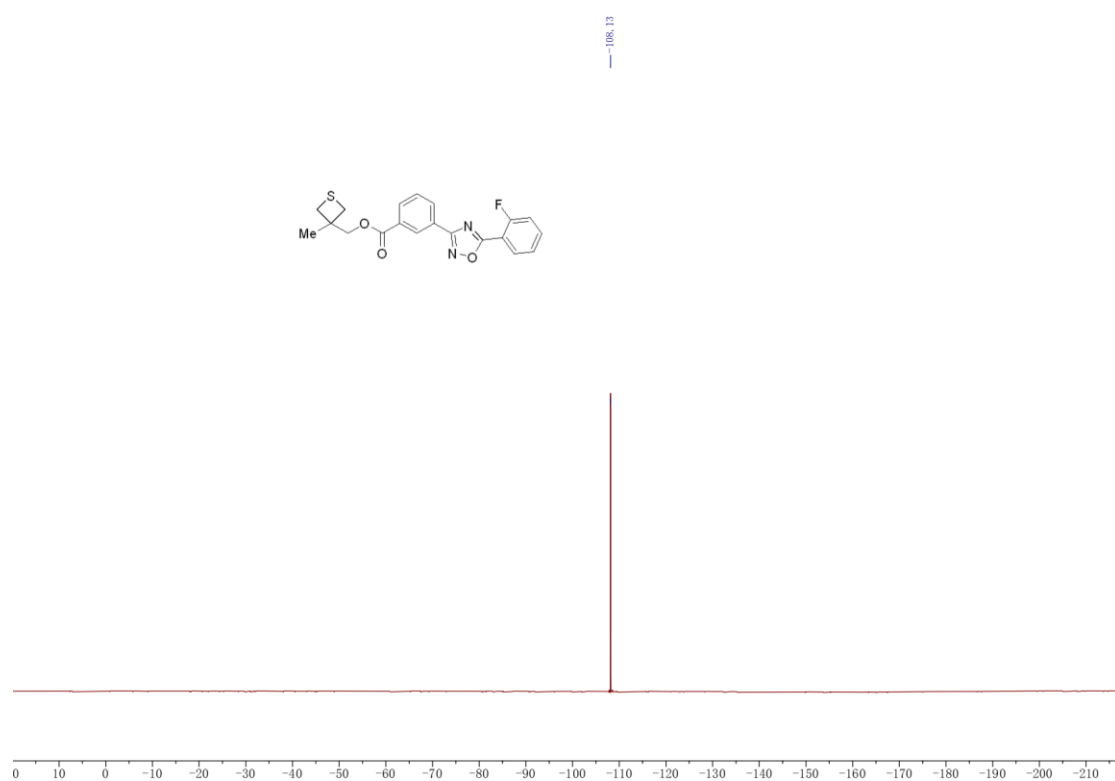
¹H NMR spectrum of 55



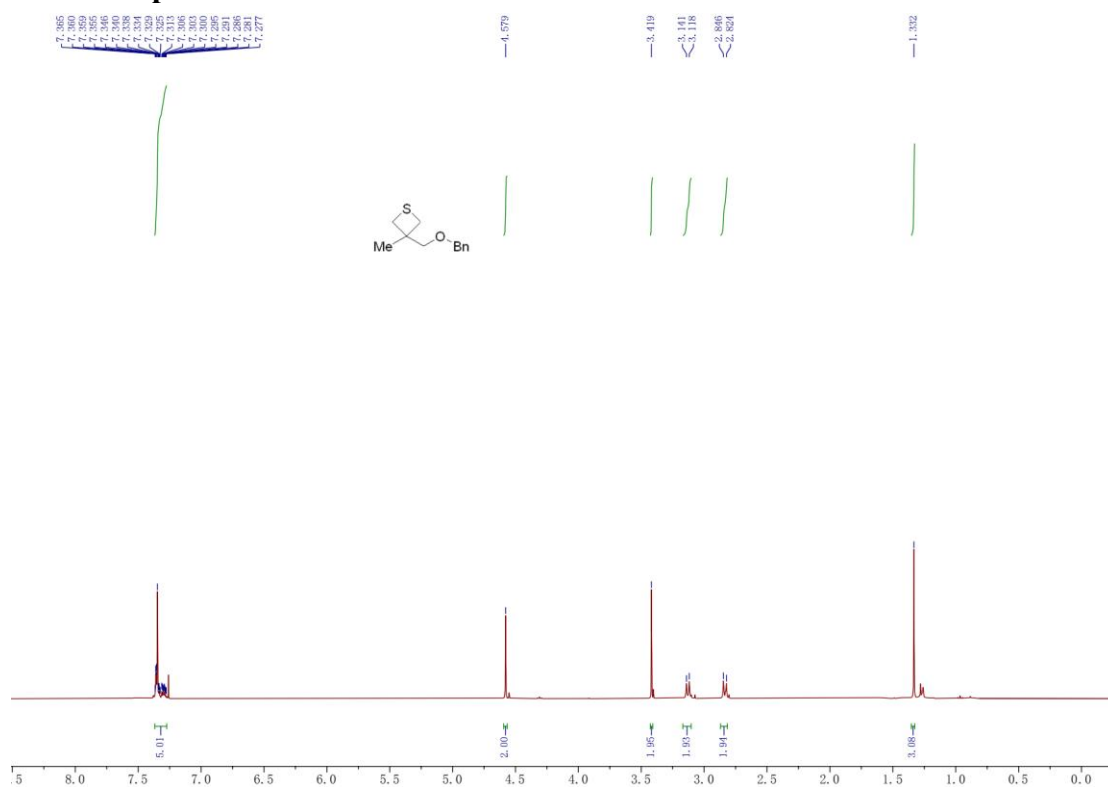
¹³C NMR spectrum of 55



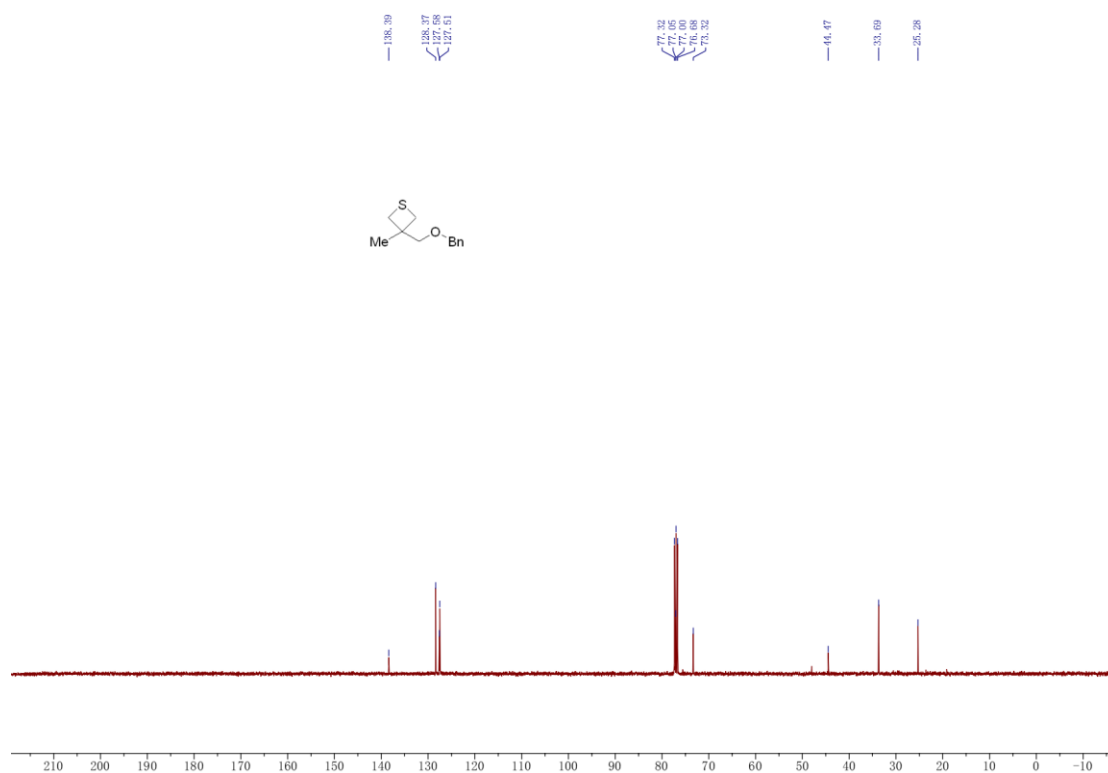
¹⁹F NMR spectrum of 55



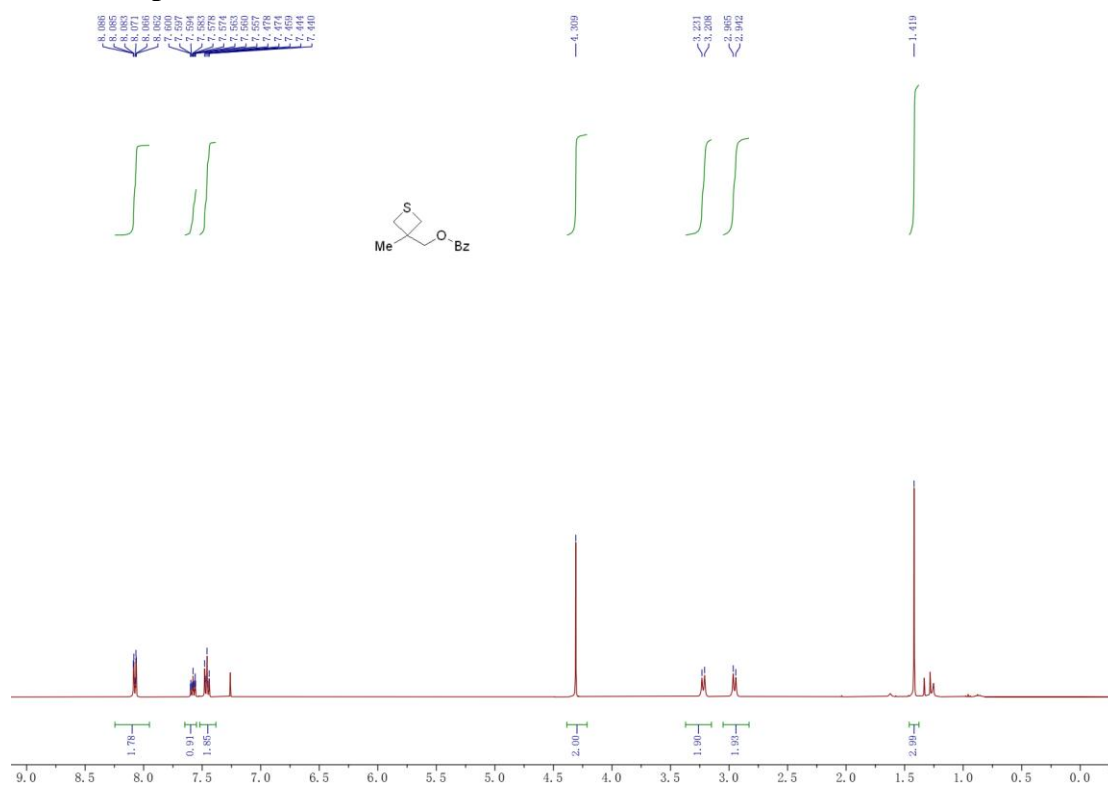
¹H NMR spectrum of 56



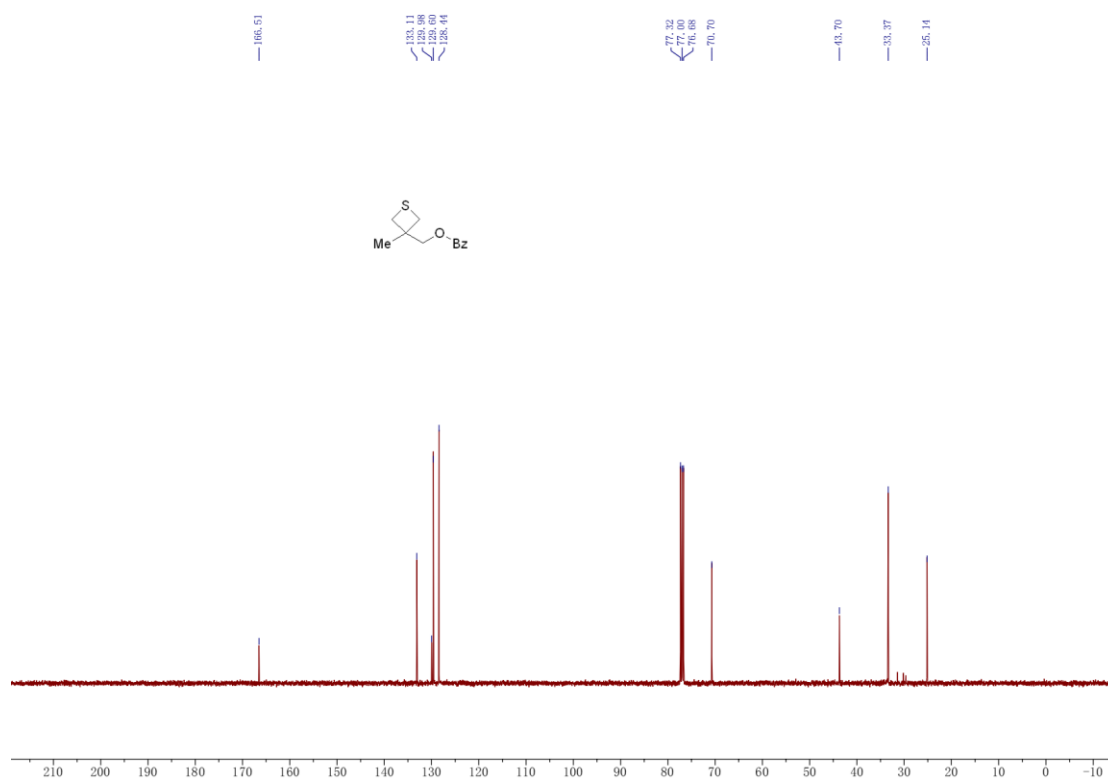
¹³C NMR spectrum of 56



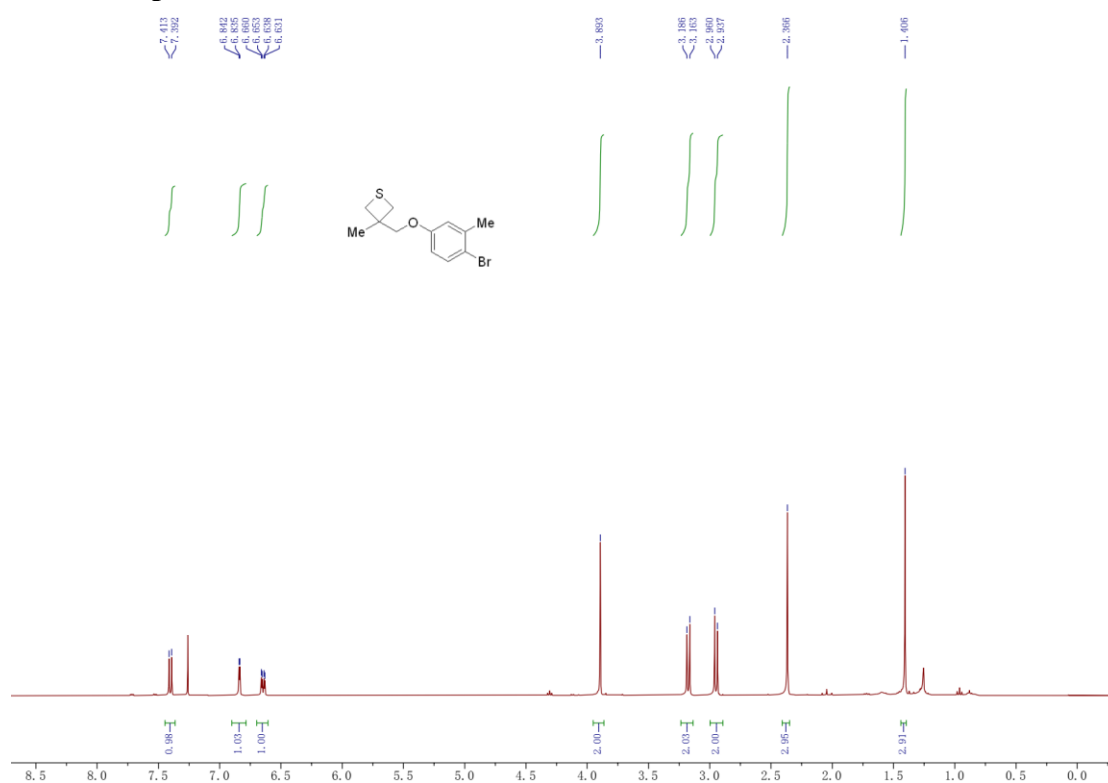
¹H NMR spectrum of 57



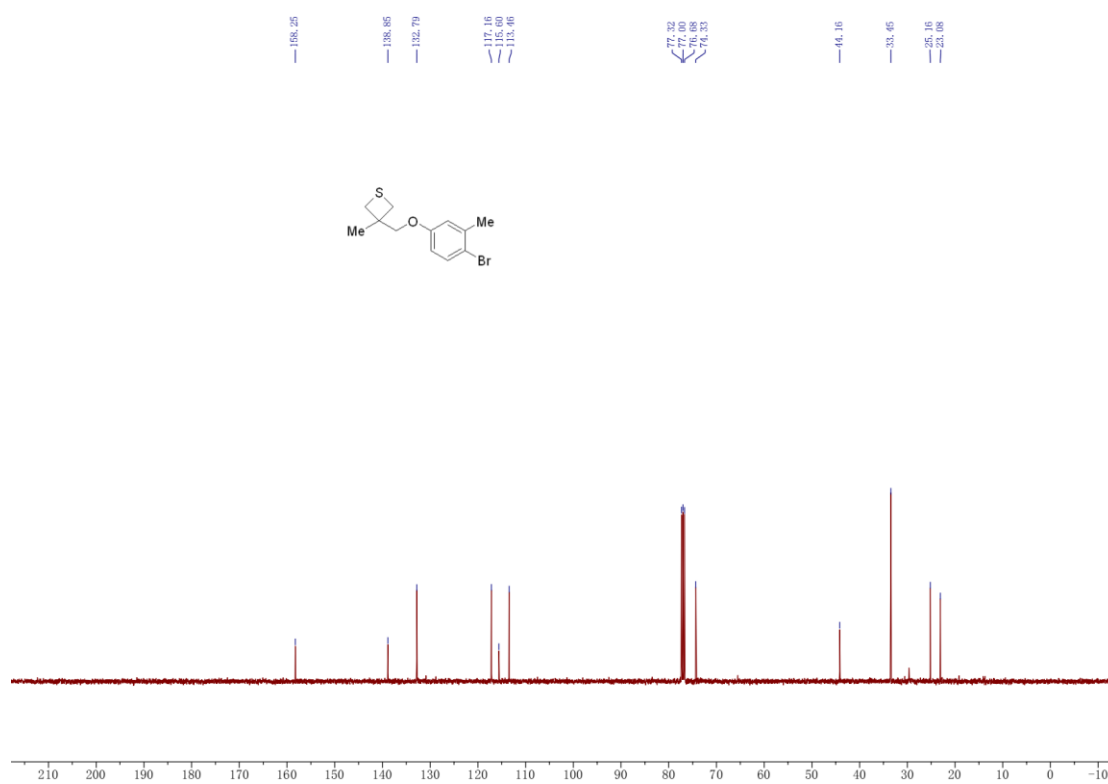
¹³C NMR spectrum of 57



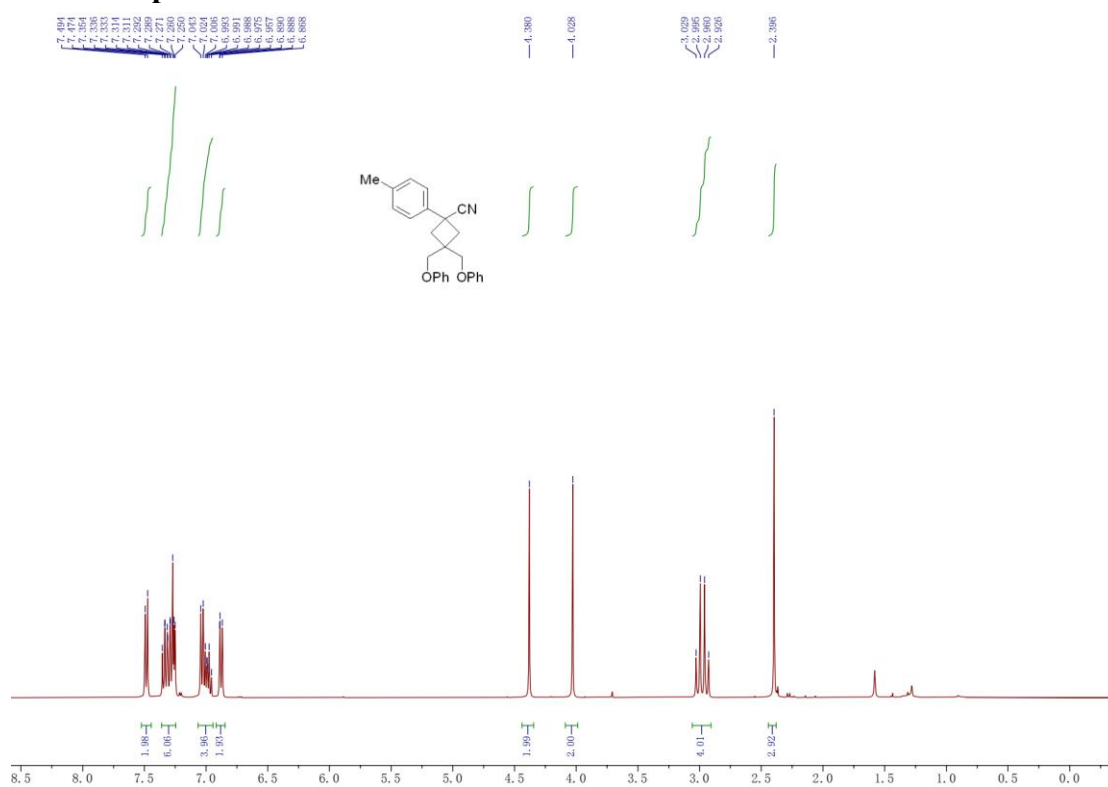
¹H NMR spectrum of 59



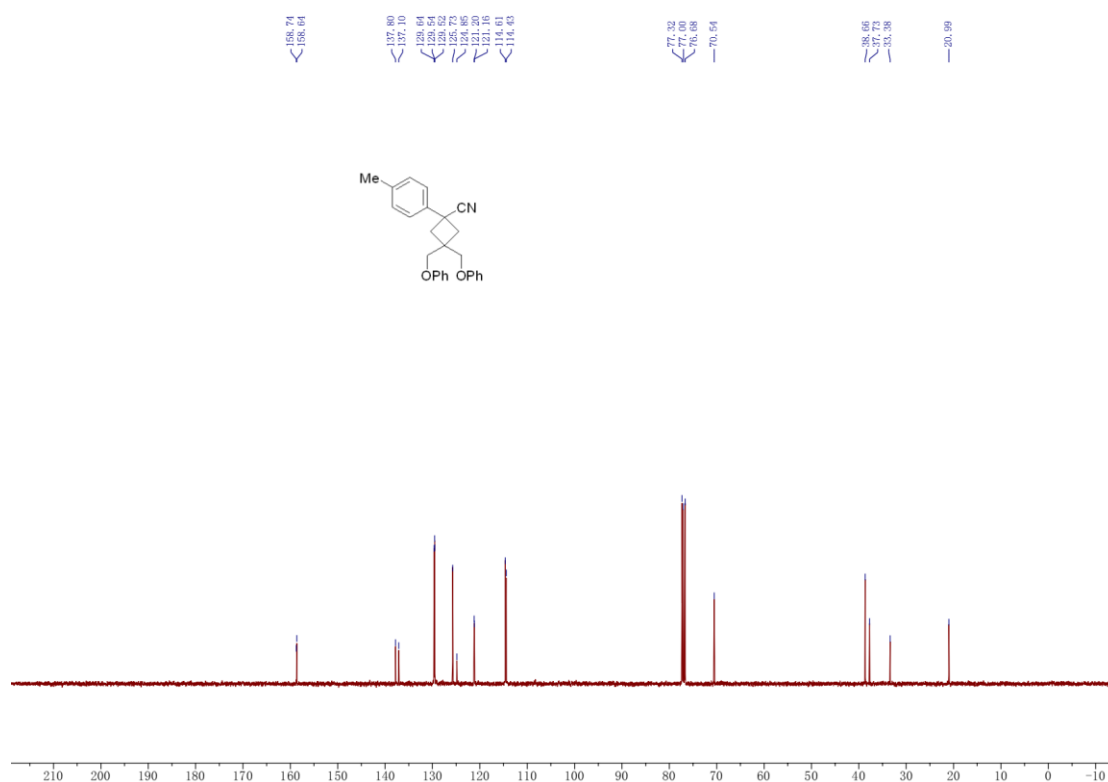
¹³C NMR spectrum of 59



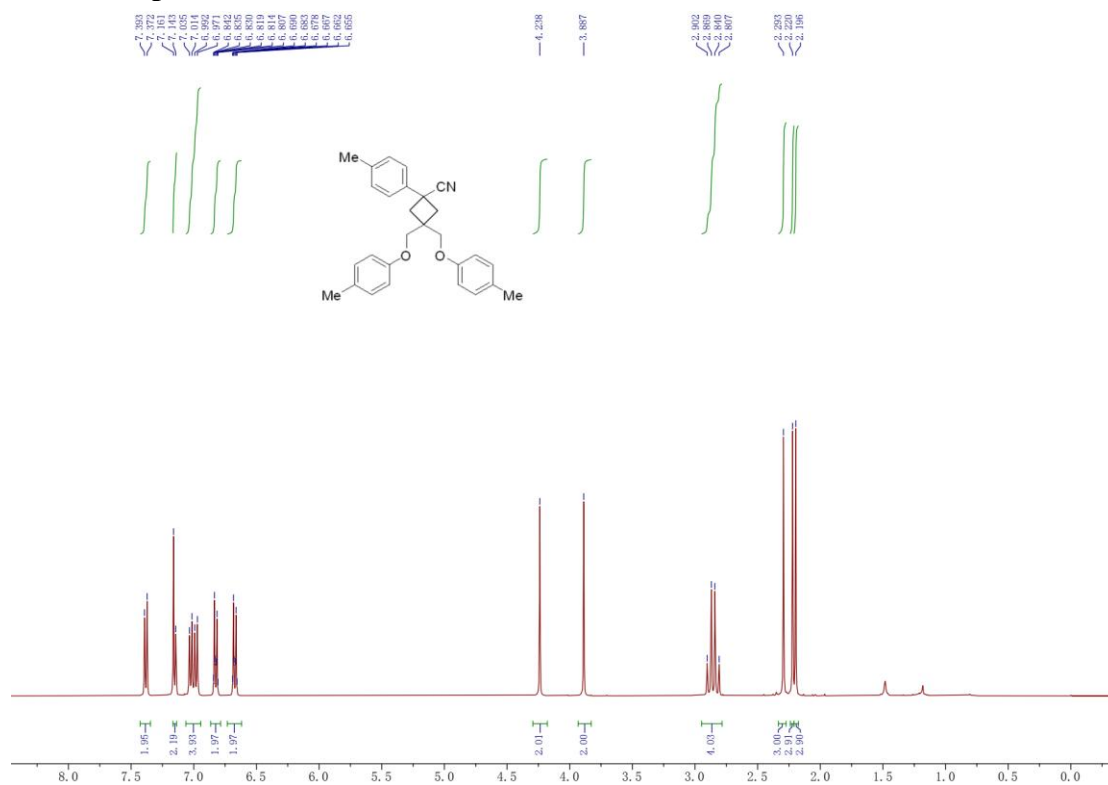
¹H NMR spectrum of 60



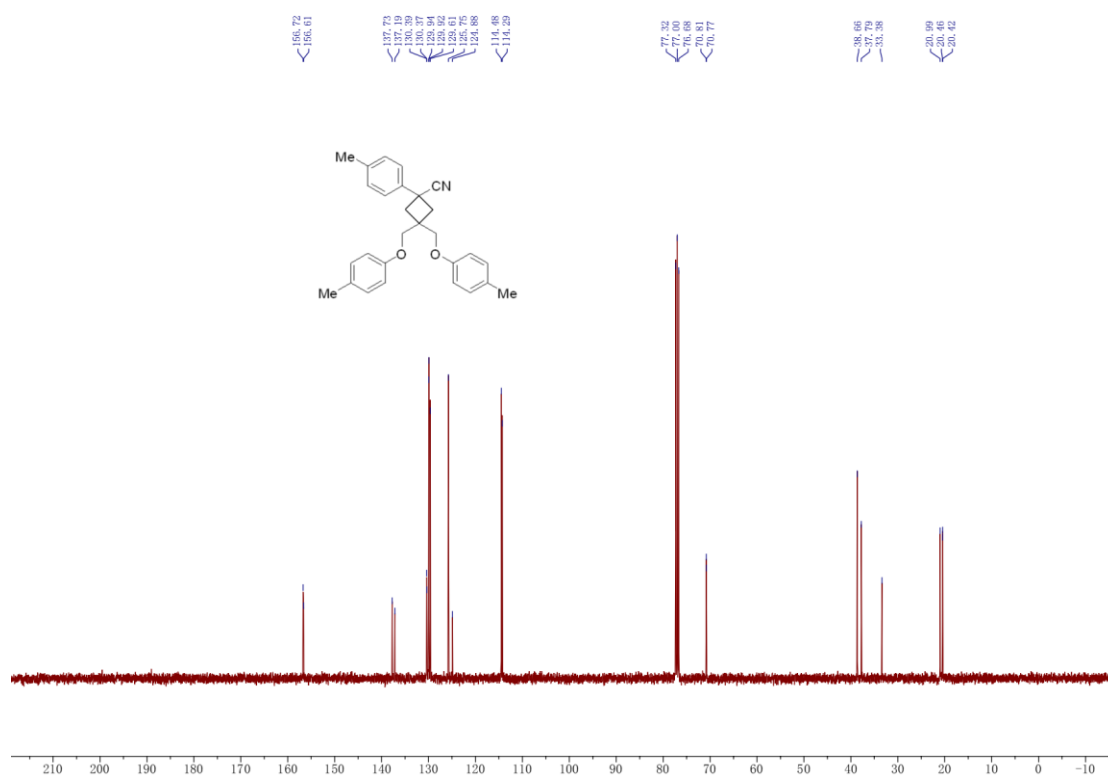
¹³C NMR spectrum of 60



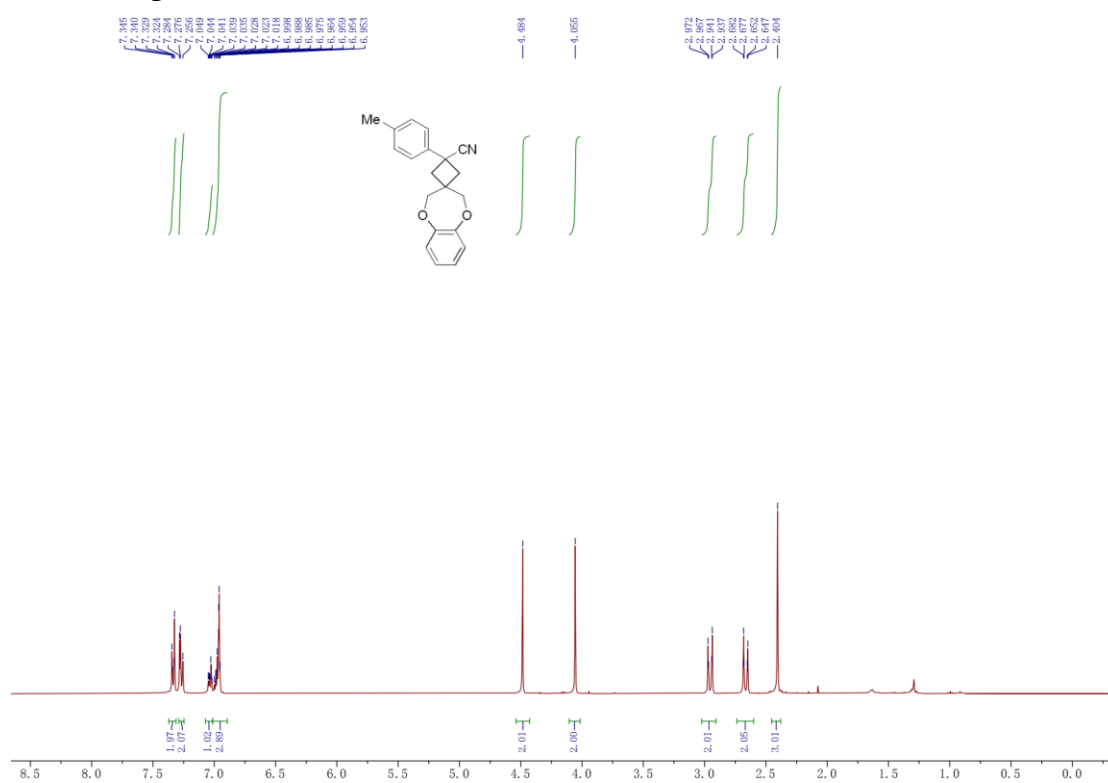
¹H NMR spectrum of 61



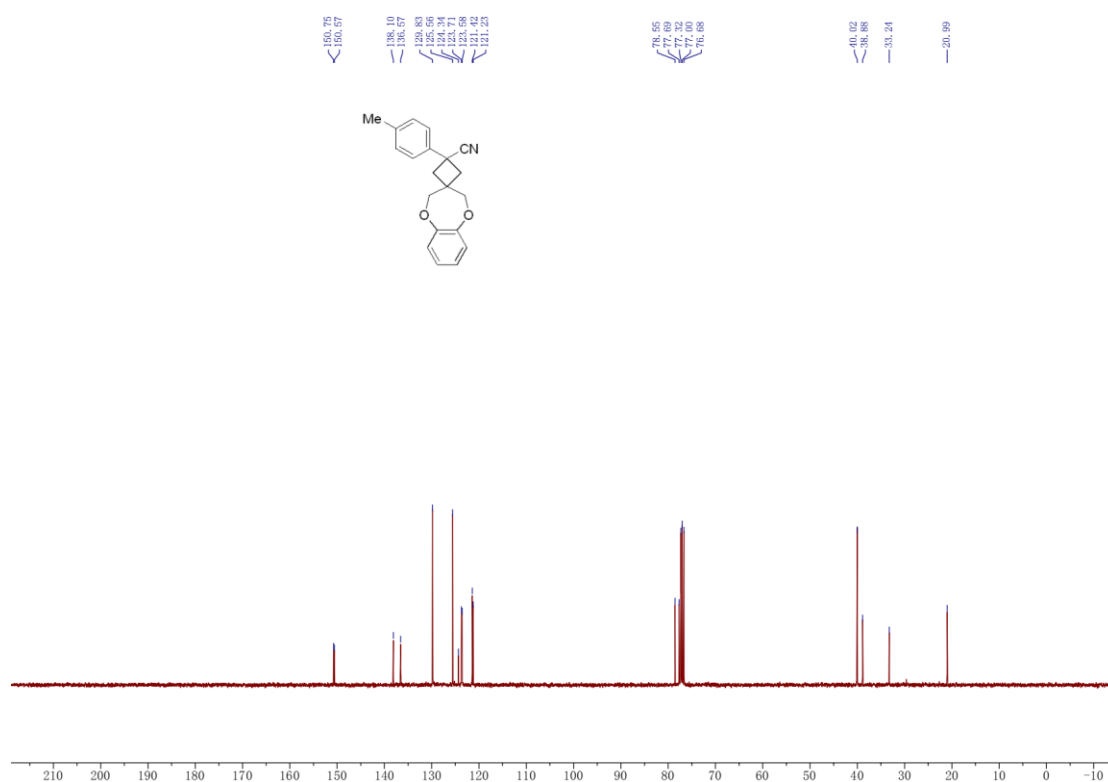
¹³C NMR spectrum of 61



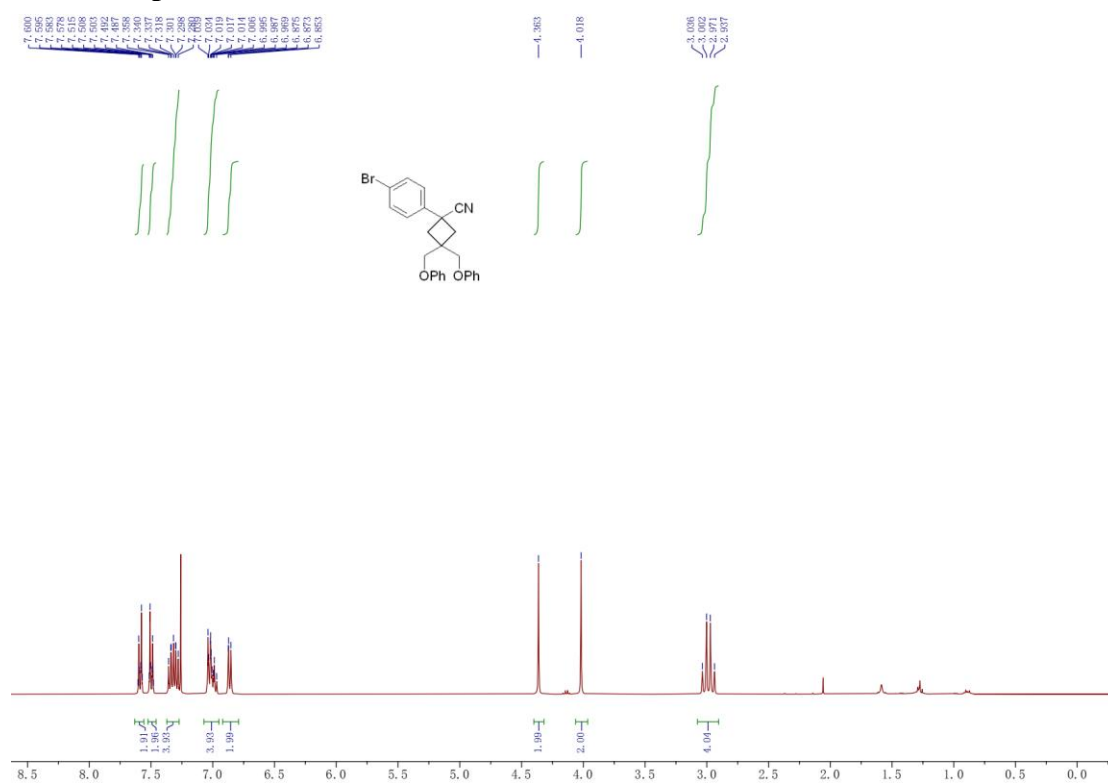
¹H NMR spectrum of 62



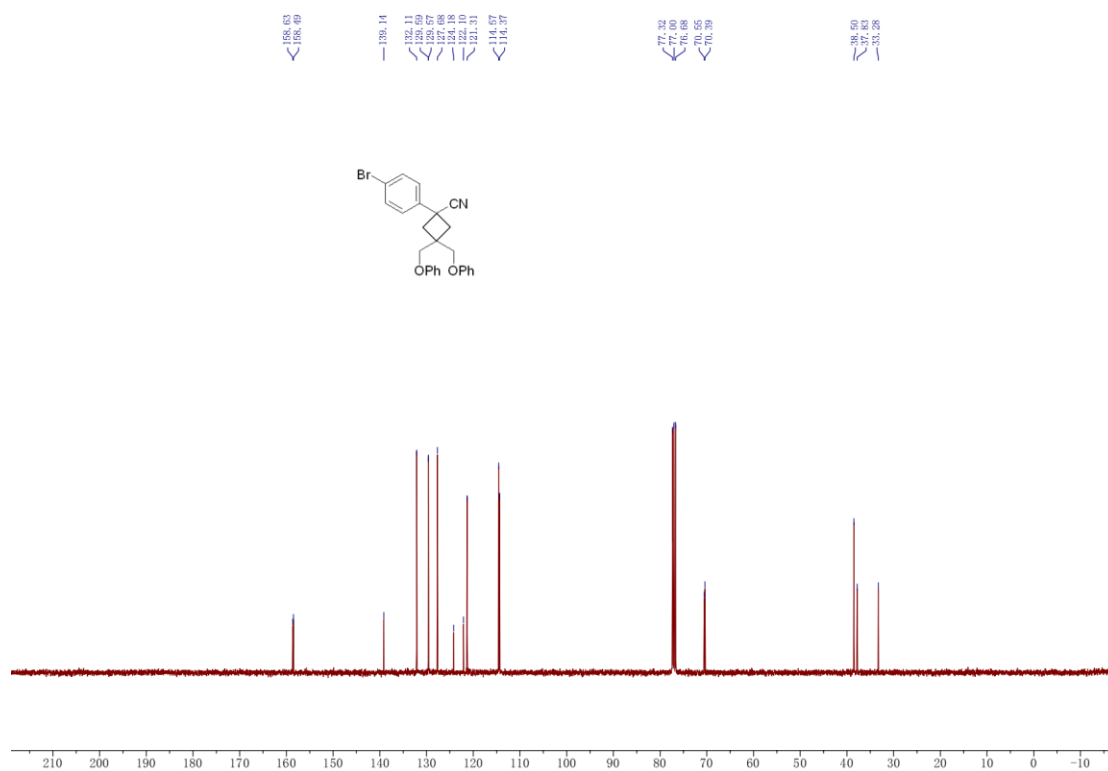
¹³C NMR spectrum of 62



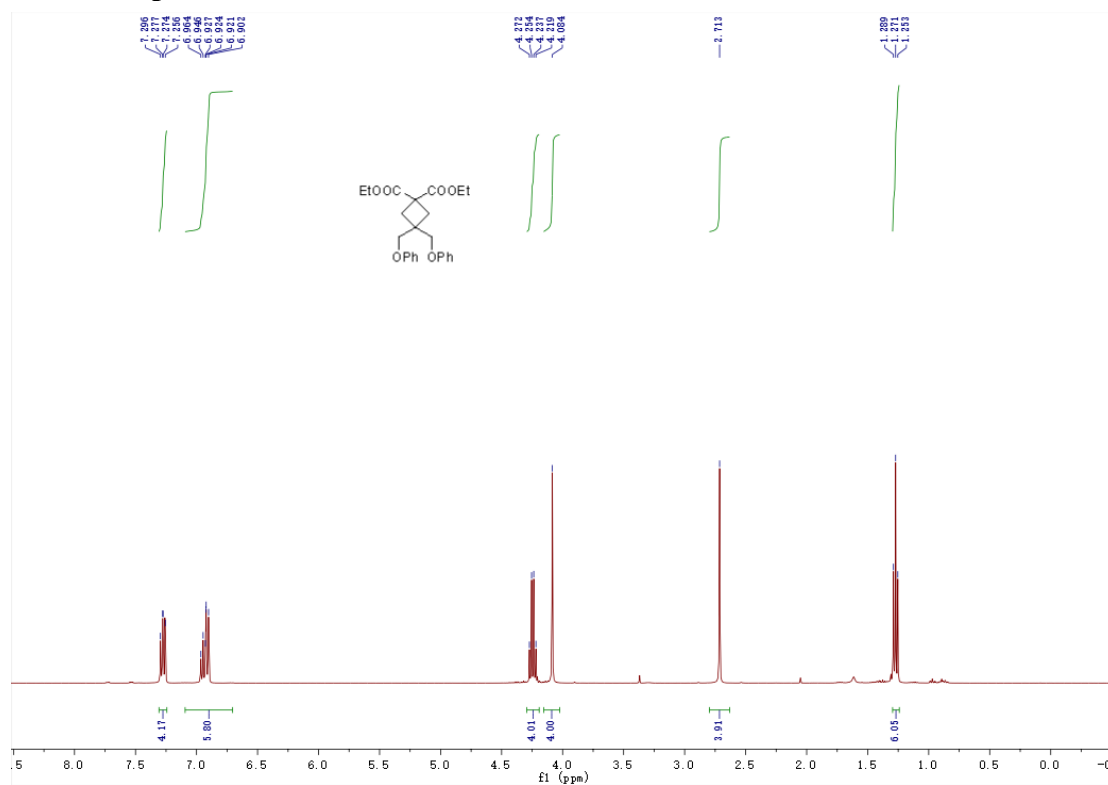
¹H NMR spectrum of 63



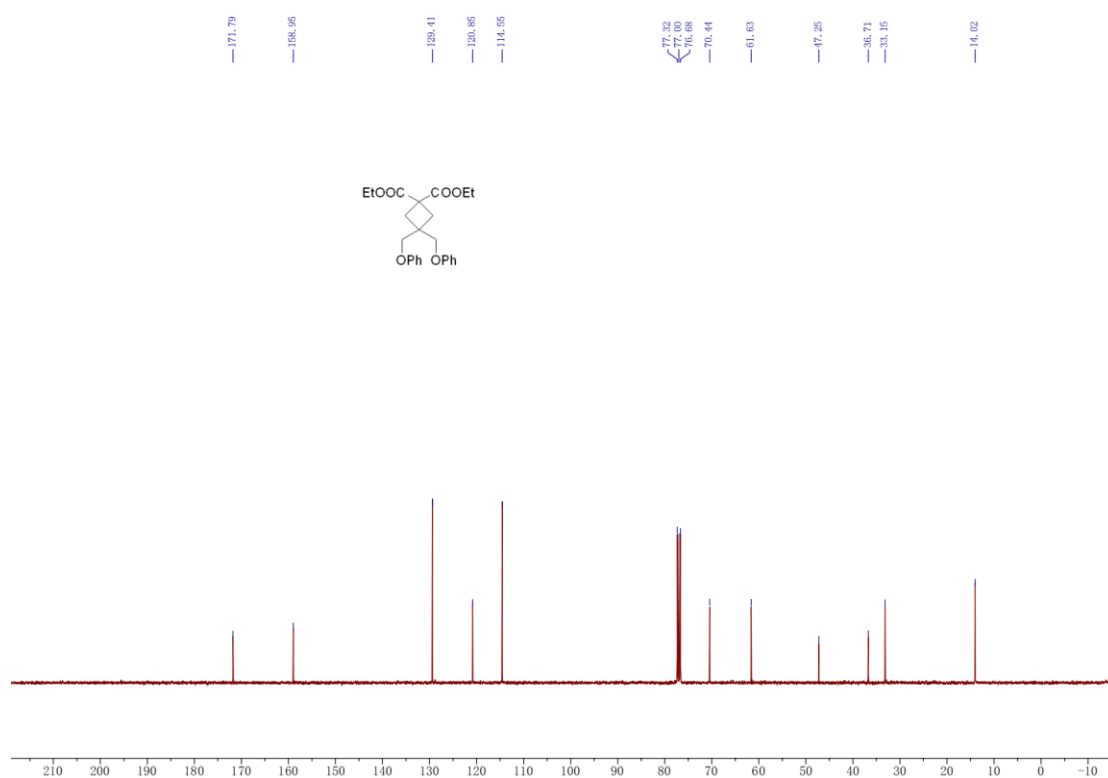
¹³C NMR spectrum of 63



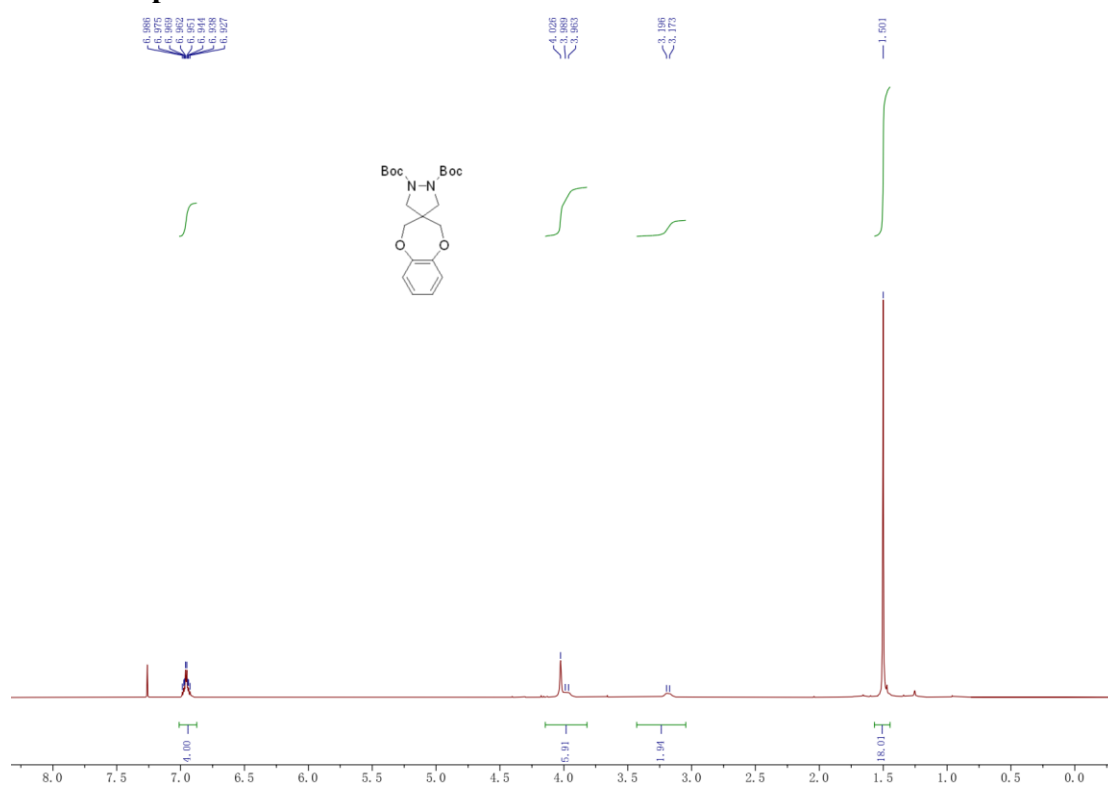
¹H NMR spectrum of 64



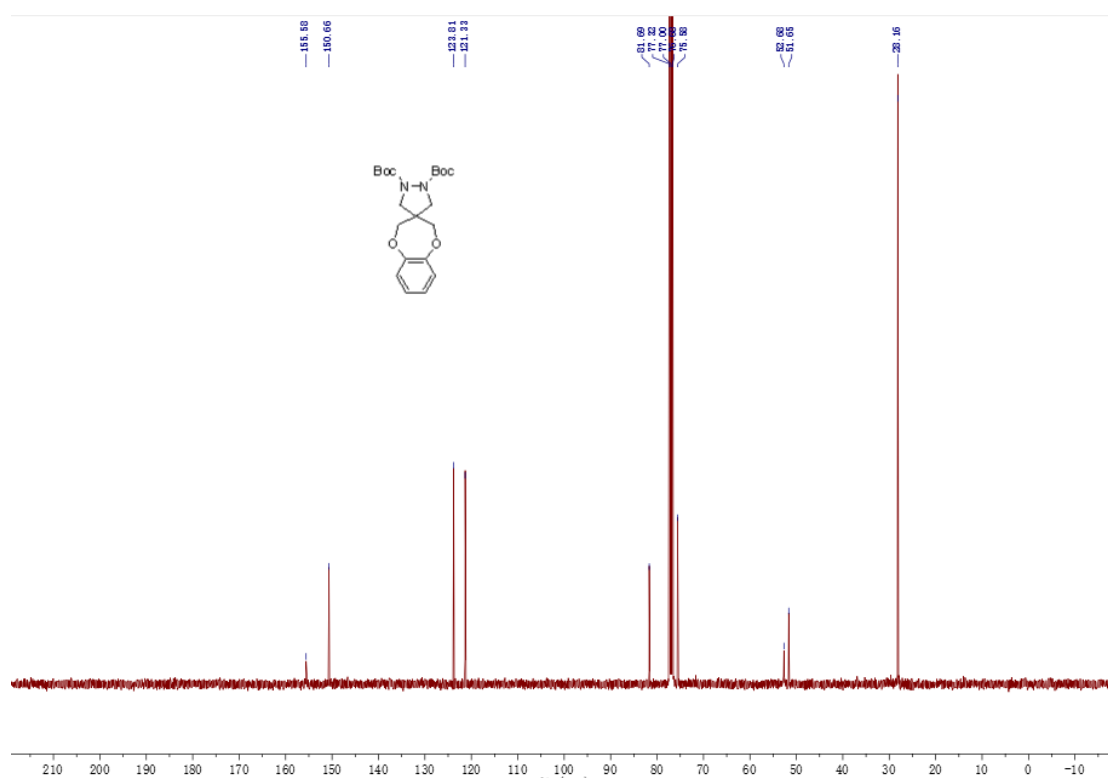
¹³C NMR spectrum of 64



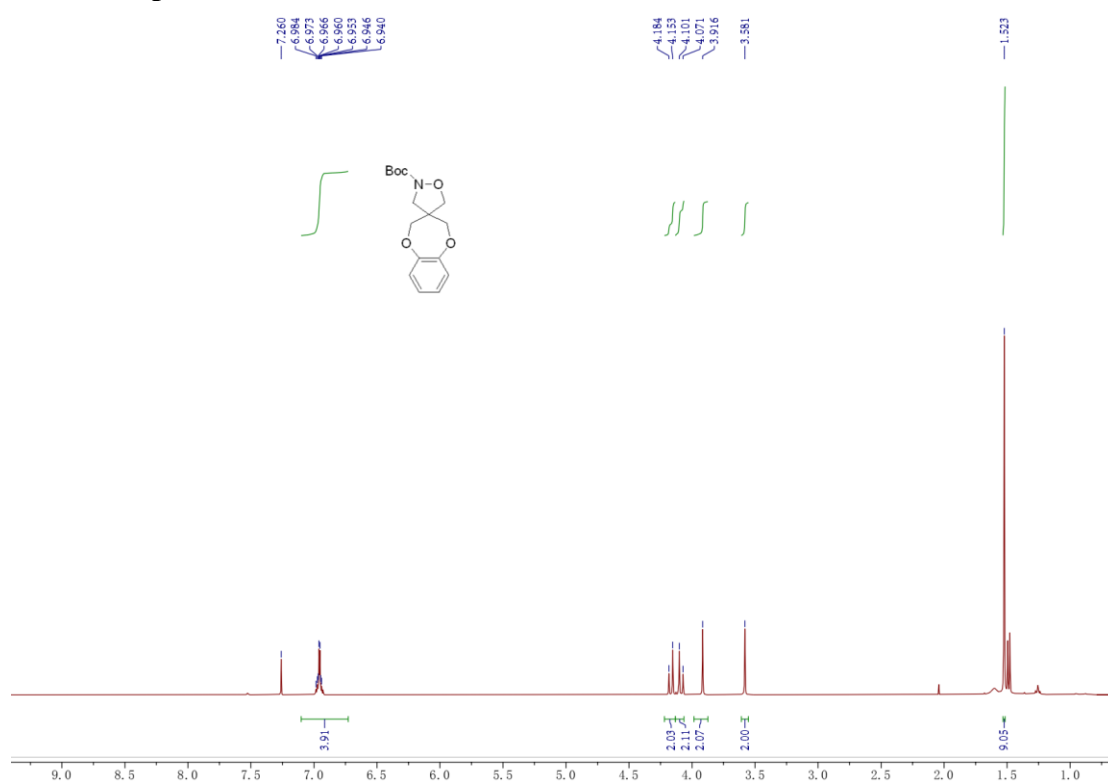
¹H NMR spectrum of 66



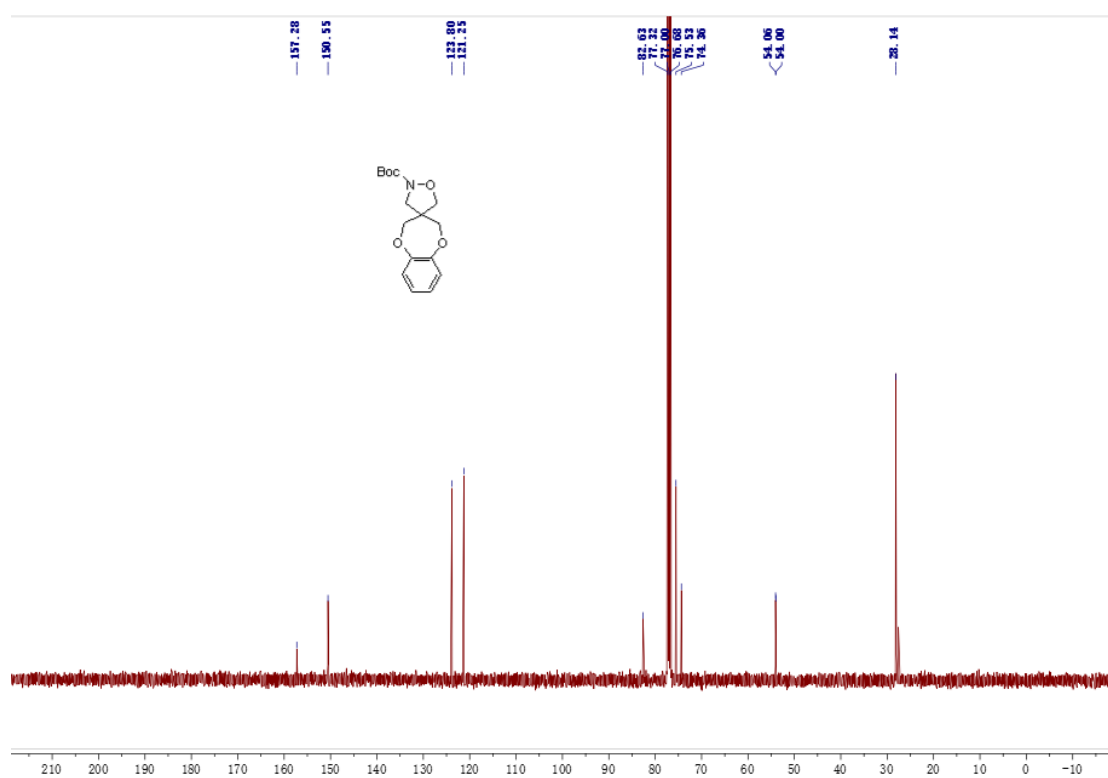
¹³C NMR spectrum of 66



¹H NMR spectrum of 67



¹³C NMR spectrum of 67



[illegible]

Chemical structure of the compound is shown above the spectrum. The structure is a substituted benzamide derivative, specifically 2-(4-(2-(4-((3-((4-phenylbutoxy)methyl)azetidin-1-yl)phenyl)-2-methyl-1,3-dioxan-6-yl)phenyl)-2-oxoethyl)benzamide.

The spectrum displays chemical shifts (ppm) on the x-axis, ranging from 0 to 210. Key peaks are labeled with their corresponding chemical shifts:

- 175.64
- 172.65
- 150.69
- 141.76
- 128.38
- 128.27
- 128.25
- 128.12
- 128.15
- 111.67
- 77.21
- 77.00
- 76.79
- 76.58
- 70.29
- 54.90
- 50.21
- 32.19
- 31.90
- 31.07
- 29.89
- 29.64
- 8.95

The spectrum shows a complex pattern of peaks, indicating the presence of multiple functional groups and structural elements in the compound.

Chemical structure of compound 10: COC(=O)N1CC(COC2=CC=CC=C2)C1Cc3c[nH]c4ccccc34

¹H NMR spectrum (CDCl₃) of compound 10. The x-axis represents the chemical shift in ppm, ranging from -0.1 to 10.0. The spectrum shows several peaks corresponding to the structure, with integration values indicated below the baseline.

Chemical structure of compound 10 is shown above the spectrum.

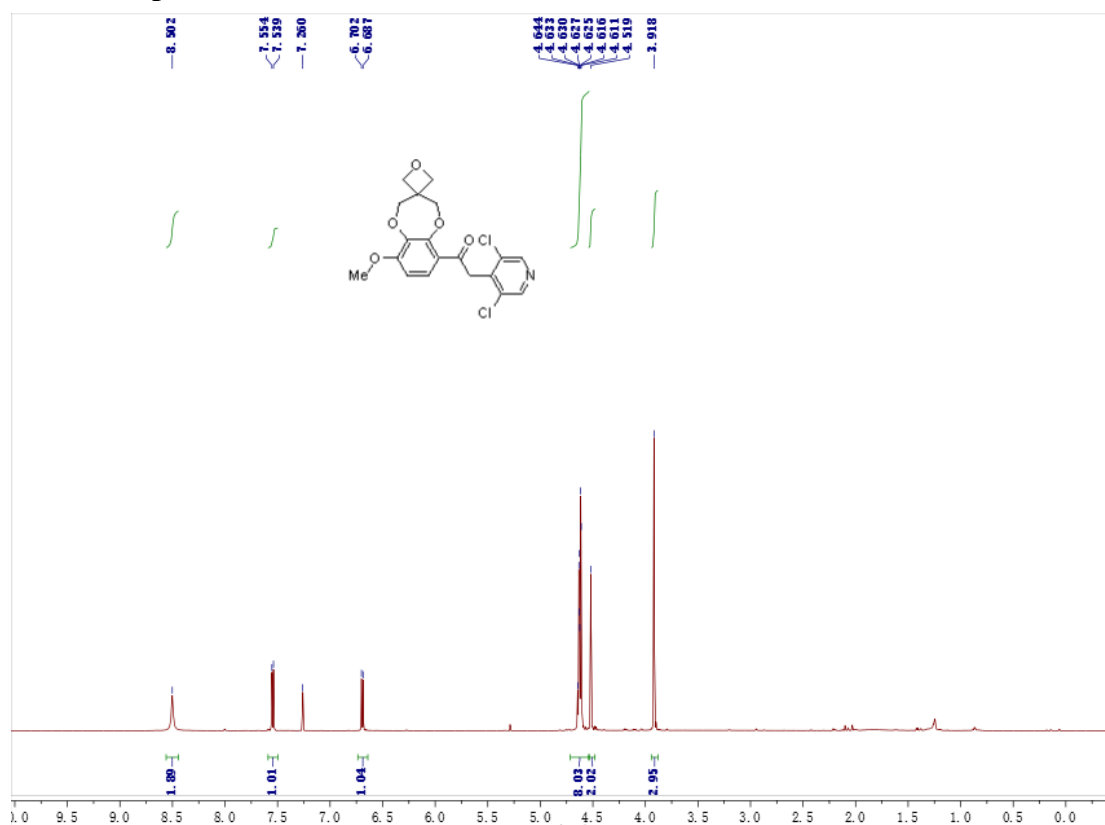
Integration values (from left to right): 0.95, 0.97, 3.12, 3.07, 0.94, 0.93, 3.92, 3.92, 3.98, 4.04, 1.00, 1.91, 2.04.

Chemical structure of the compound is shown above the spectrum. The spectrum displays peaks corresponding to the chemical structure, with the following chemical shifts (ppm) labeled above the peaks:

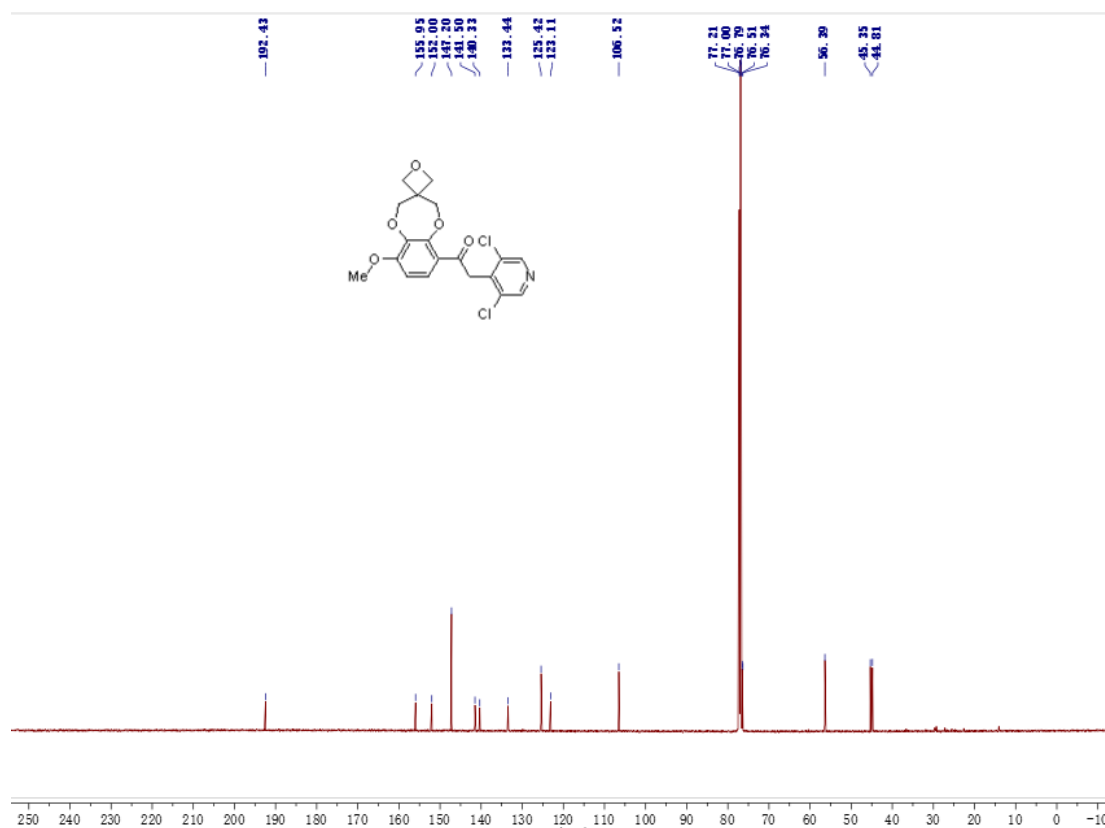
172.55, 141.89, 136.07, 128.43, 128.29, 127.38, 125.74, 122.69, 121.89, 118.28, 118.56, 111.18, 111.12, 77.32, 77.00, 76.68, 72.75, 70.65, 70.17, 55.96, 55.93, 51.58, 32.26, 31.16, 30.58, 26.08.

COC(=O)N1CCOC1COCCc2ccccc2C3=CNc4ccccc34

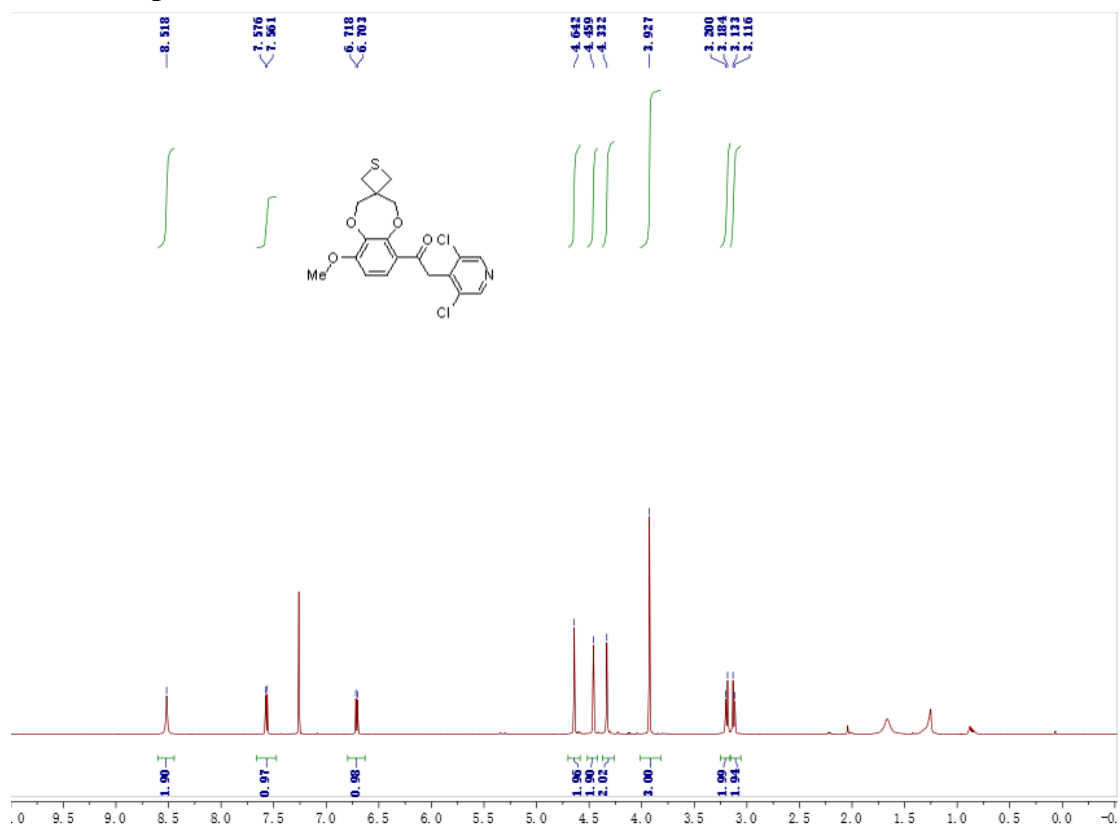
¹H NMR spectrum of 70



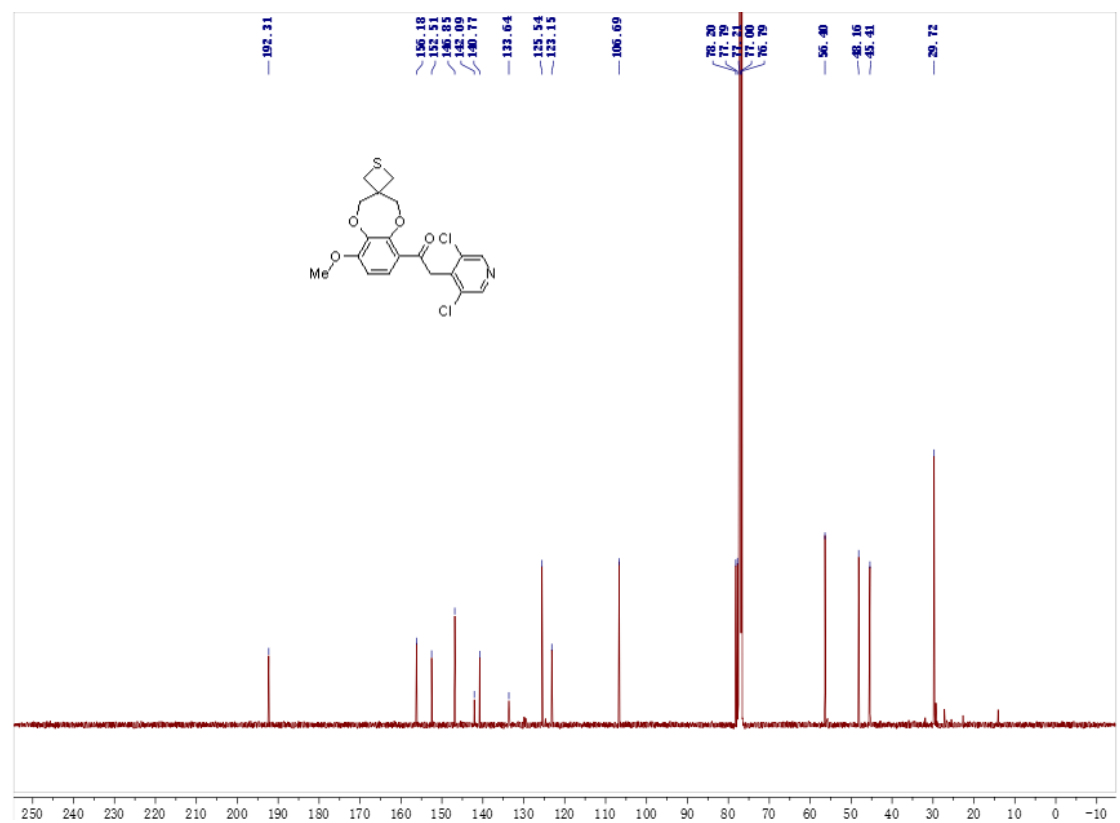
¹³C NMR spectrum of 70



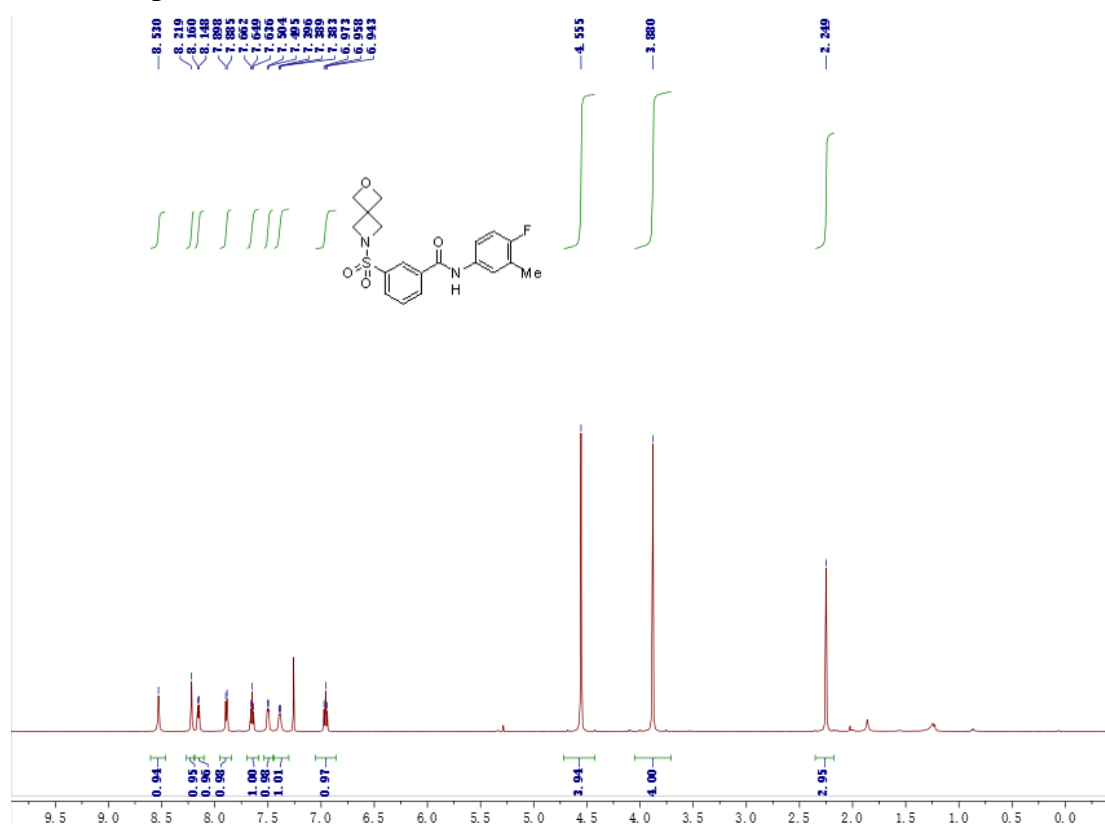
¹H NMR spectrum of 71



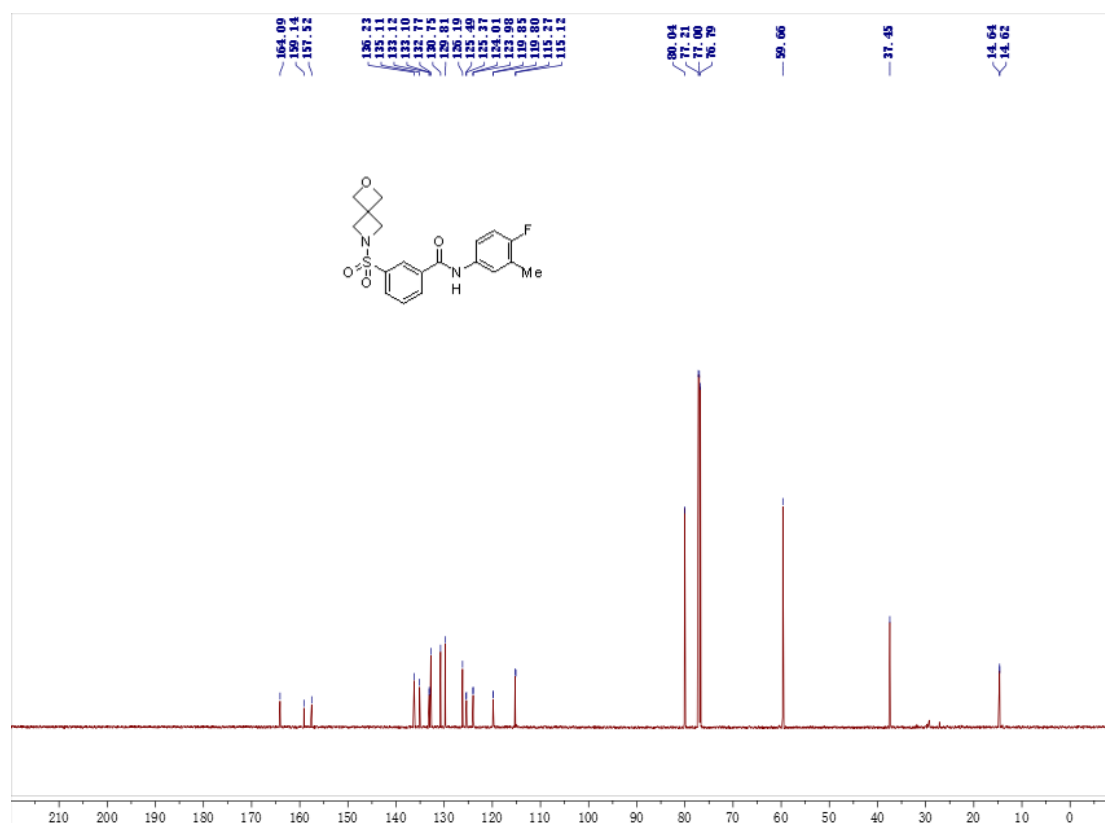
¹³C NMR spectrum of 71



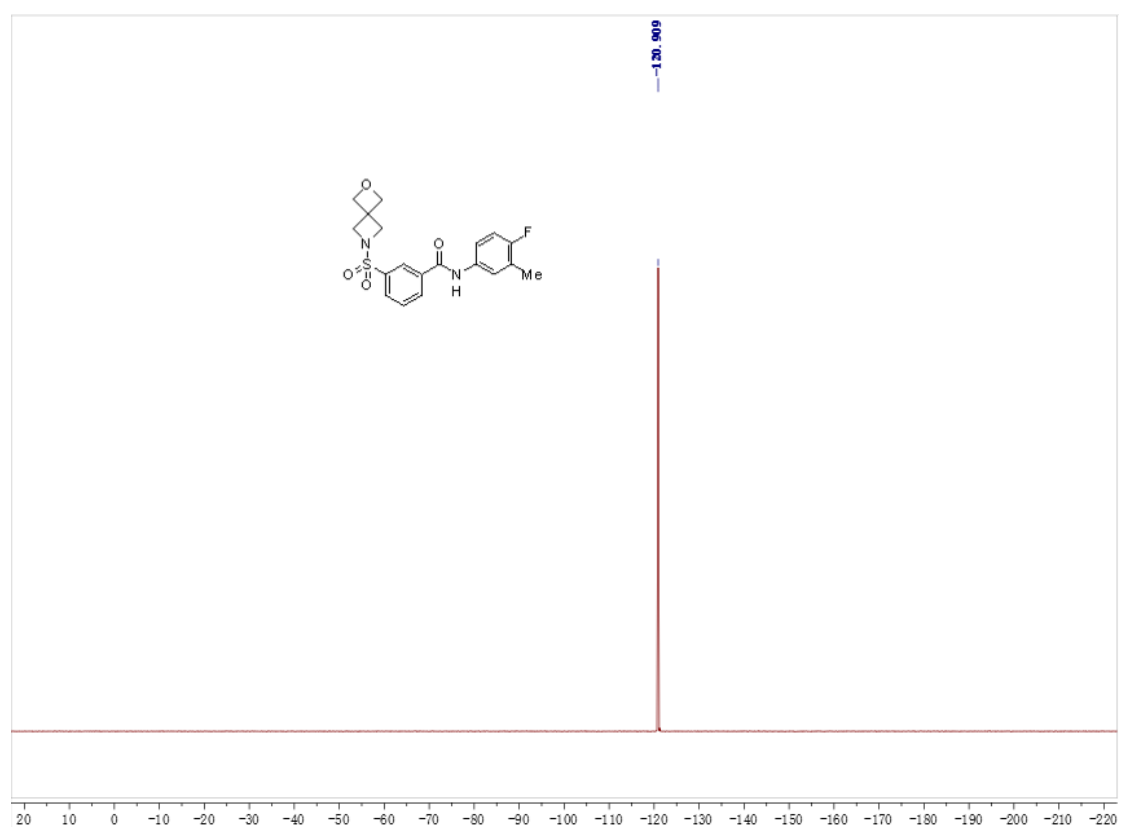
¹H NMR spectrum of 72



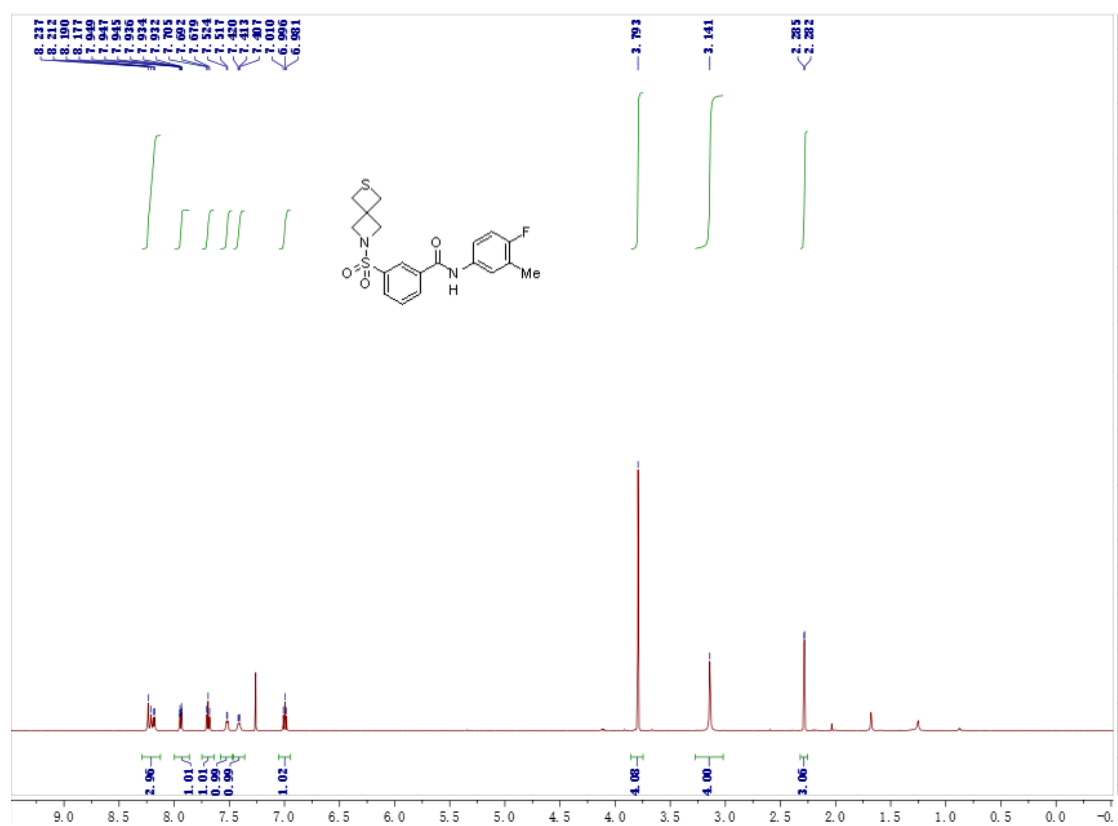
¹³C NMR spectrum of 72



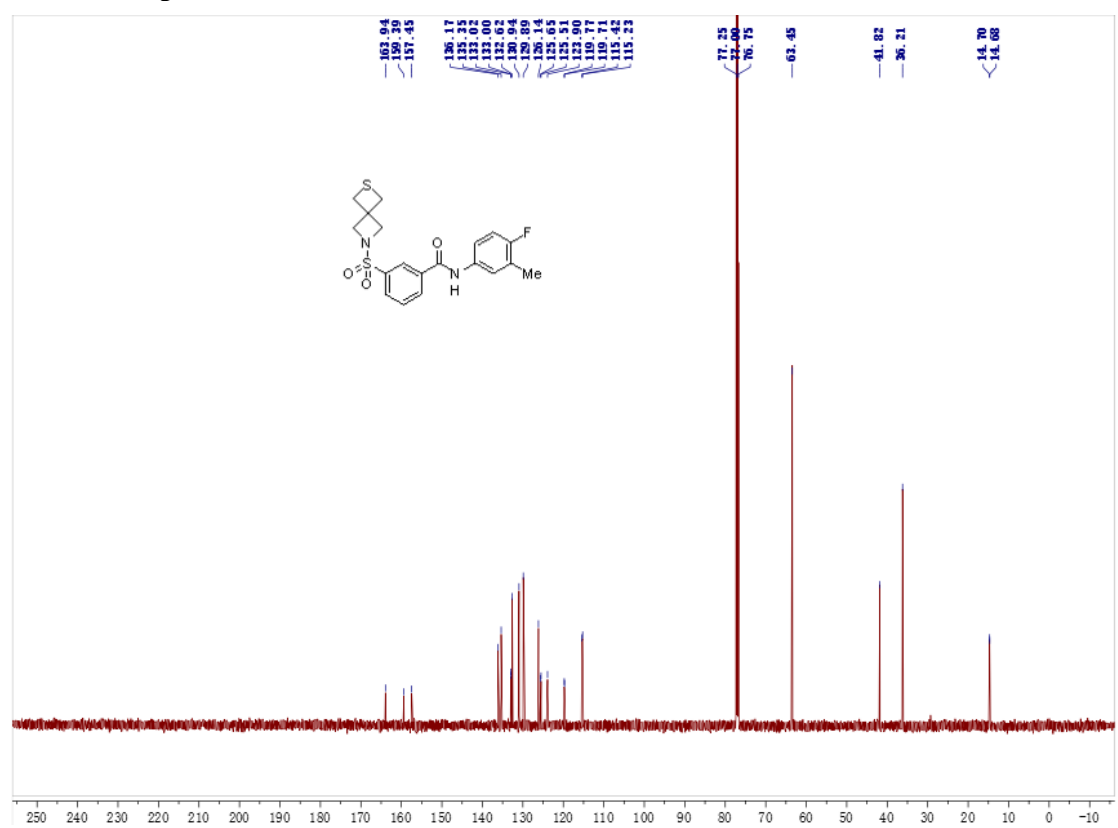
^{19}F NMR spectrum of 72



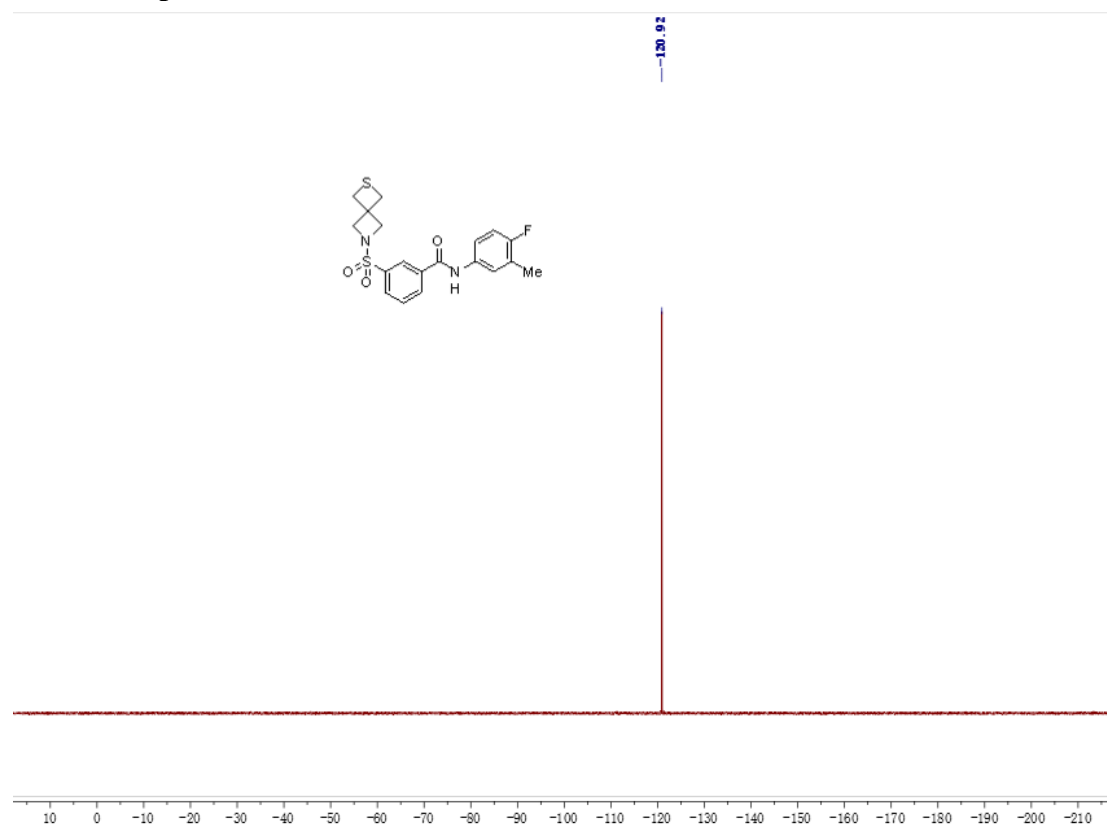
¹H NMR spectrum of 73



¹³C NMR spectrum of 73



^{19}F NMR spectrum of 73



Chemical structure: O=C1C2CCN(C2c3ccc([N+](=O)[O-])cc3F)C1

¹H NMR spectrum (ppm):

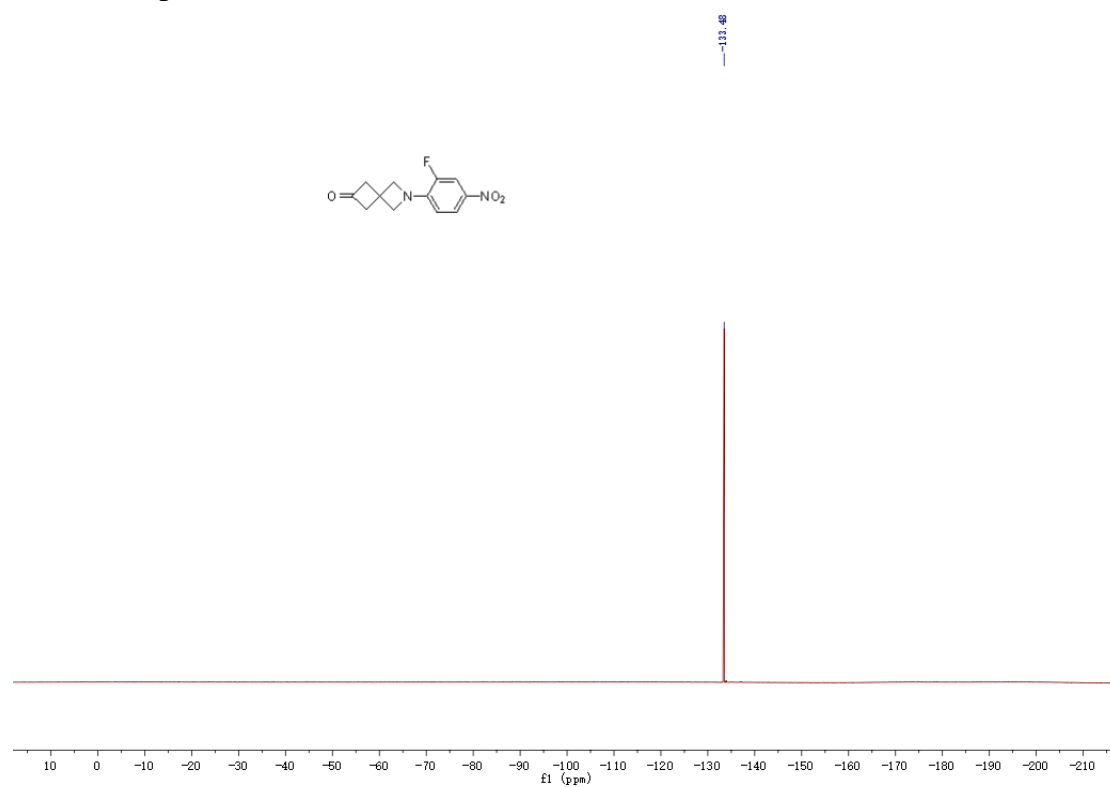
- 8.04 (d, 0.04H)
- 7.92 (d, 0.92H)
- 7.81 (t, 1.00H)
- 7.71 (t, 4.04H)
- 7.66 (t, 3.98H)
- 7.61 (t, 4.04H)
- 7.51 (t, 3.98H)
- 4.35 (d, 4.04H)
- 4.30 (d, 3.98H)
- 3.40 (s, 3.98H)
- 3.40 (s, 4.04H)

Chemical structure: O=[N+]([O-])c1ccc(N2C3CC4C(C3)CC(=O)CC4)cc1F

¹³C NMR peaks (ppm):

- 151.01
- 146.58
- 143.54
- 143.43
- 137.92
- 137.85
- 131.62
- 131.59
- 112.39
- 112.16
- 111.85
- 111.70
- 77.50
- 77.30
- 76.62
- 64.22
- 64.20
- 57.77
- 29.77
- 29.74

¹⁹F NMR spectrum of 74



Chemical structure: Fc1cc(cc(c1N2CC(F)(F)CC2)C3=CC=CC=C3[N+](=O)[O-])

¹H NMR spectrum (CDCl₃) data:

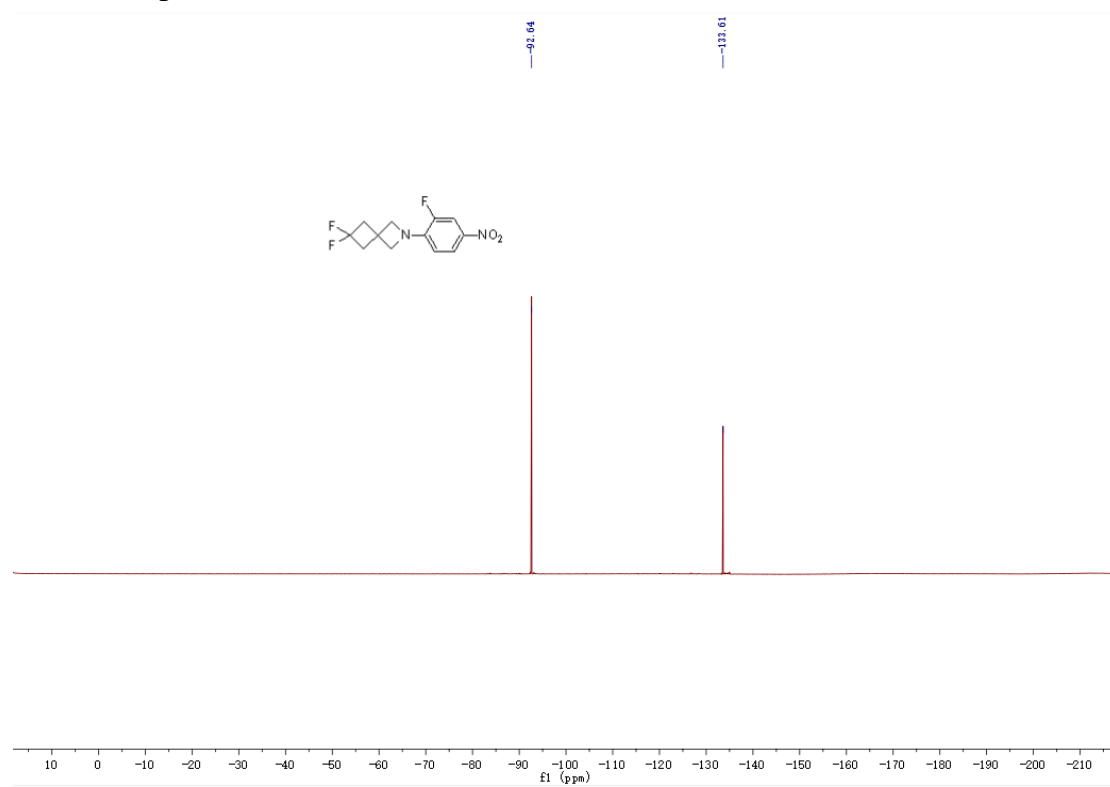
Chemical Shift (ppm)	Integration
7.80 (d)	0.94
7.78 (d)	0.91
7.25 (s)	-
6.35 (d)	1.00
4.25 (s)	4.00
2.85 (m)	4.04

Chemical structure: Fc1ccc(cc1N2CC3(C2)CC(F)(F)C3)c4ccc(cc4)[N+](=O)[O-]

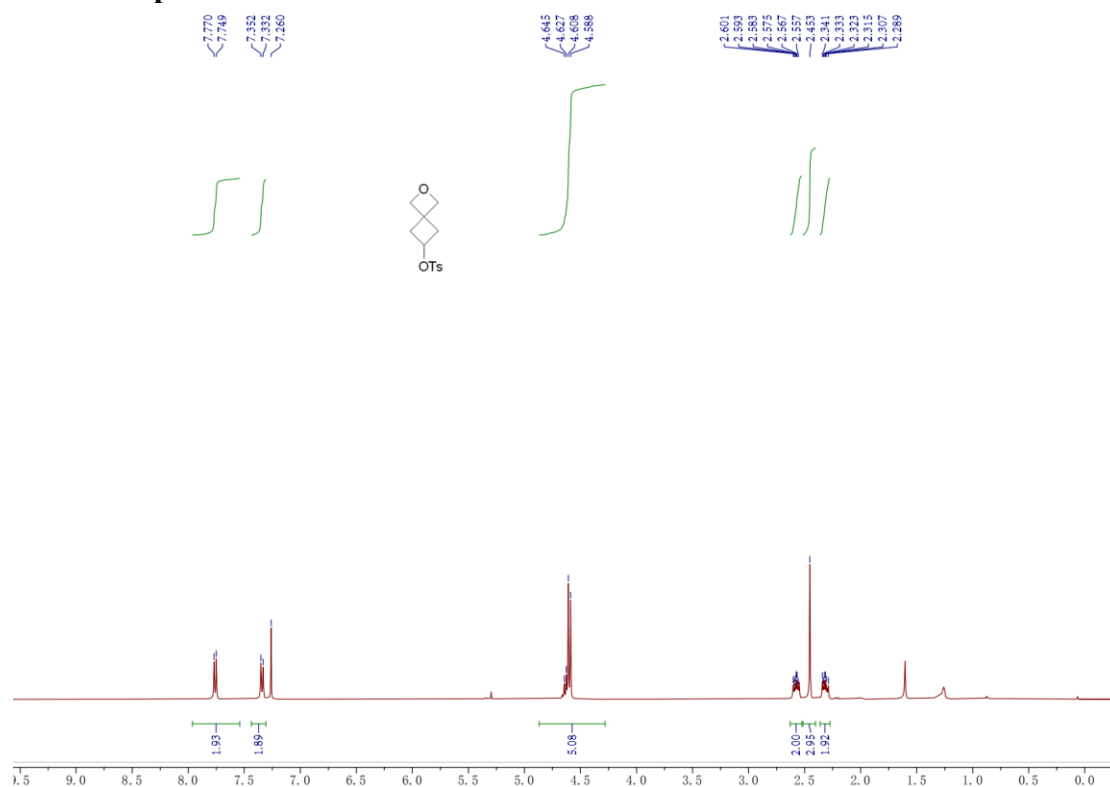
¹³C NMR spectrum (CDCl₃) showing peaks at the following chemical shifts (ppm):

- 150.93
- 149.82
- 148.82
- 143.41
- 137.64
- 137.76
- 121.61
- 121.89
- 121.91
- 118.40
- 118.63
- 118.63
- 118.63
- 112.93
- 111.65
- 111.60
- 77.25
- 76.68
- 64.08
- 64.05
- 46.09
- 46.06
- 46.63
- 29.13
- 29.07
- 29.00
- 29.00
- 28.93
- 28.90

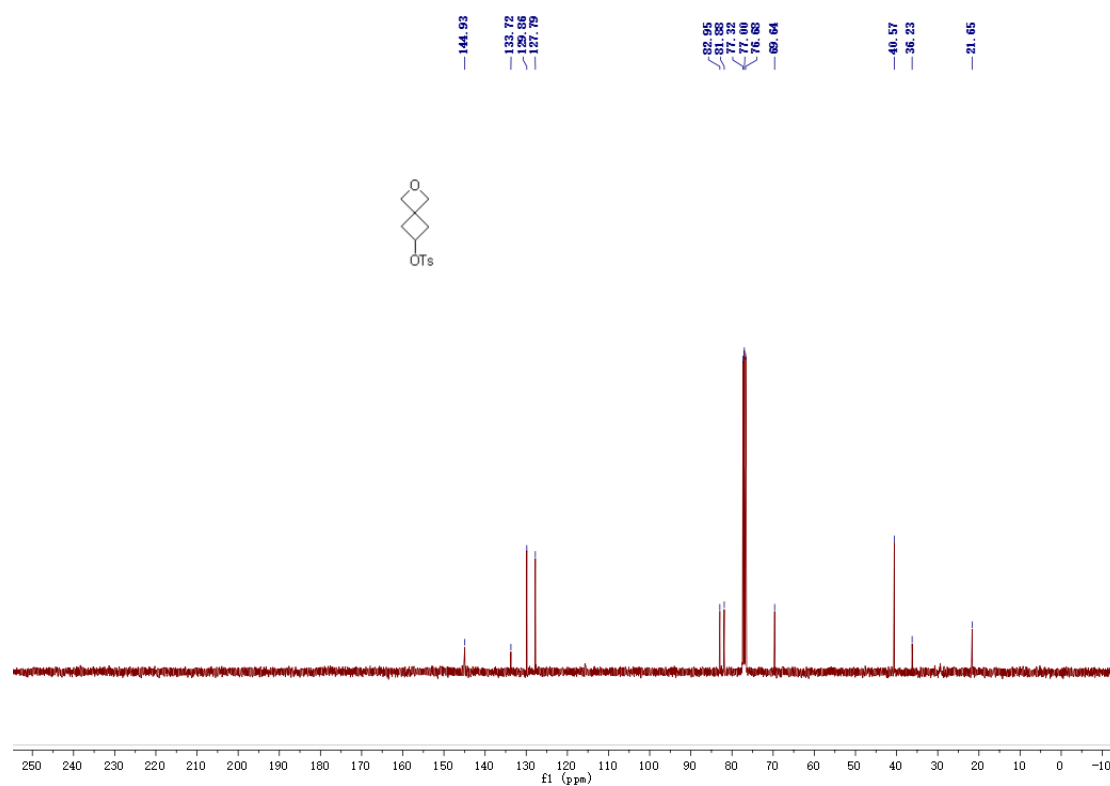
¹⁹F NMR spectrum of 7



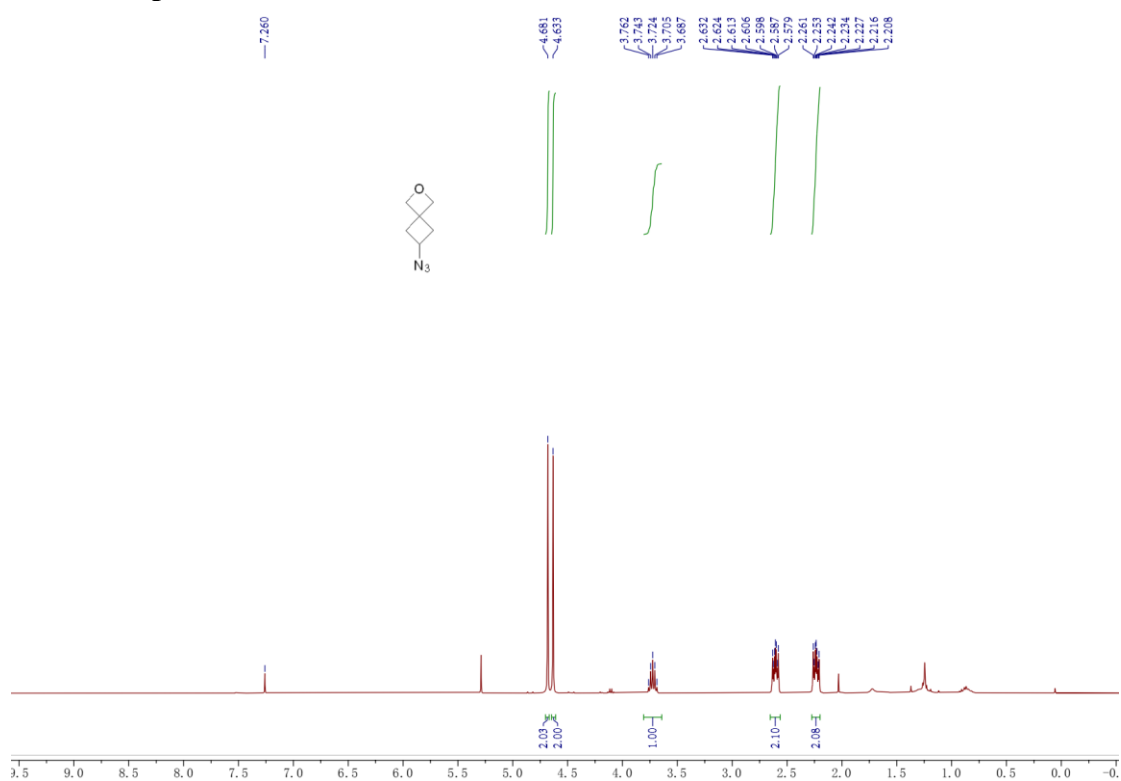
¹H NMR spectrum of 76



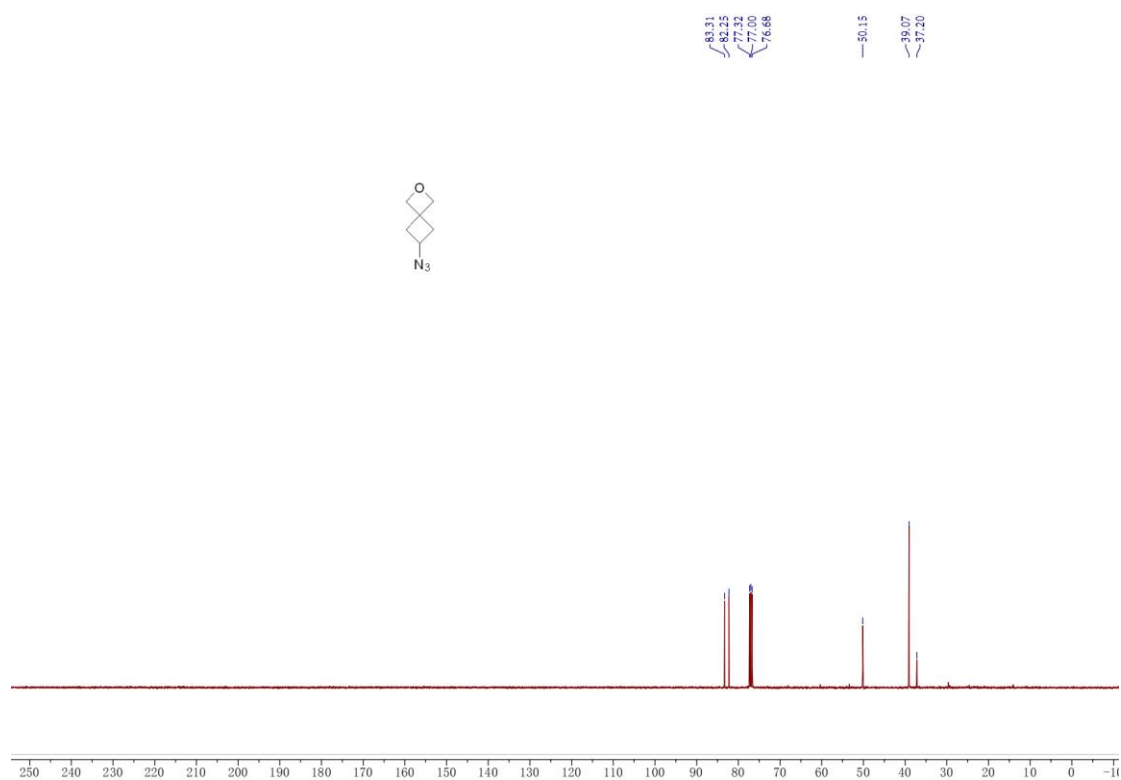
¹³C NMR spectrum of 76



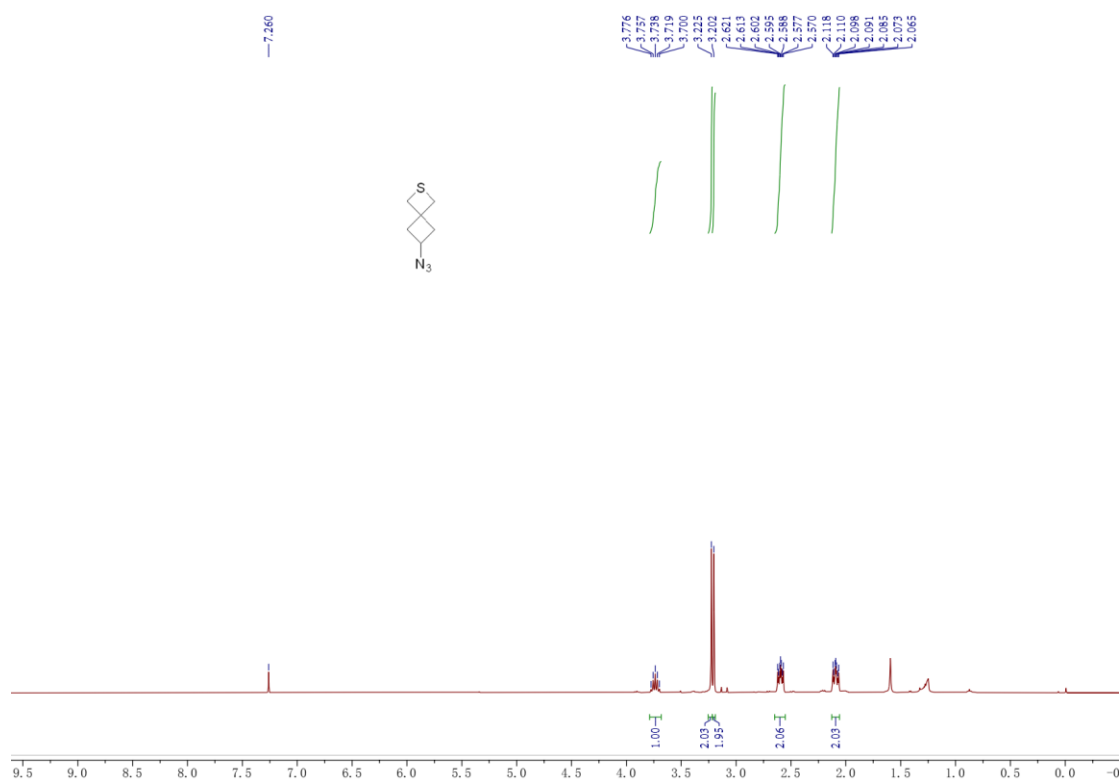
¹H NMR spectrum of 77



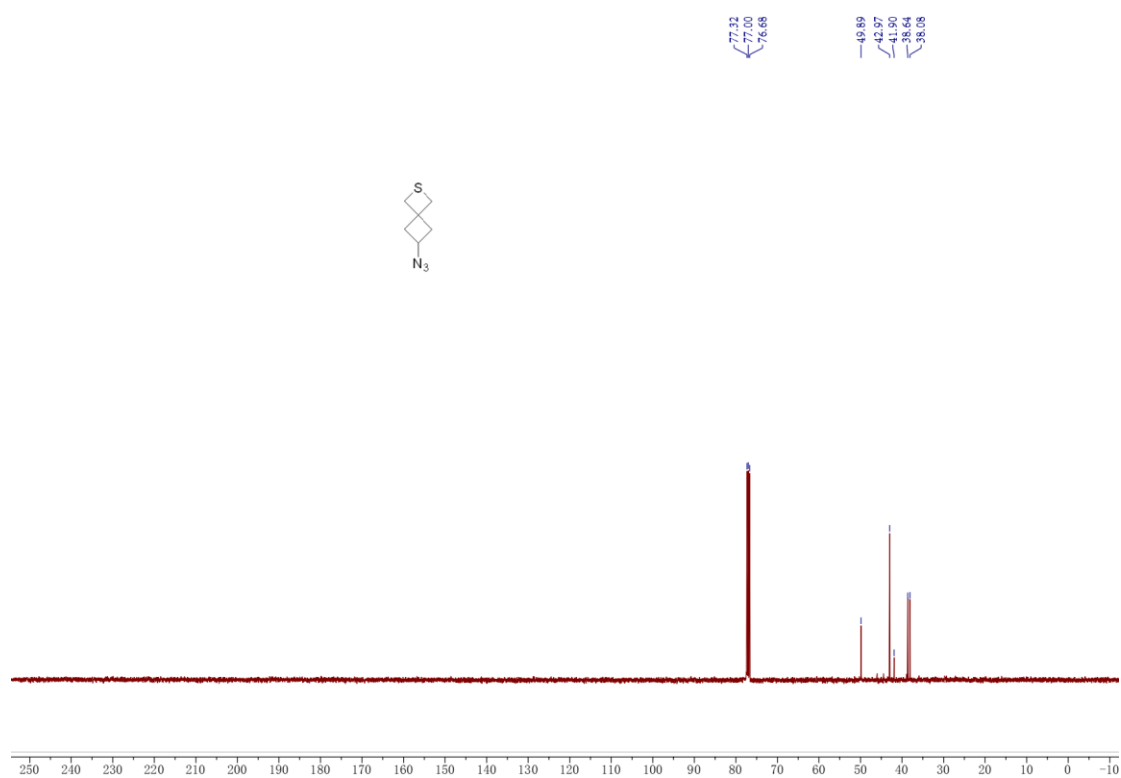
¹³C NMR spectrum of 77



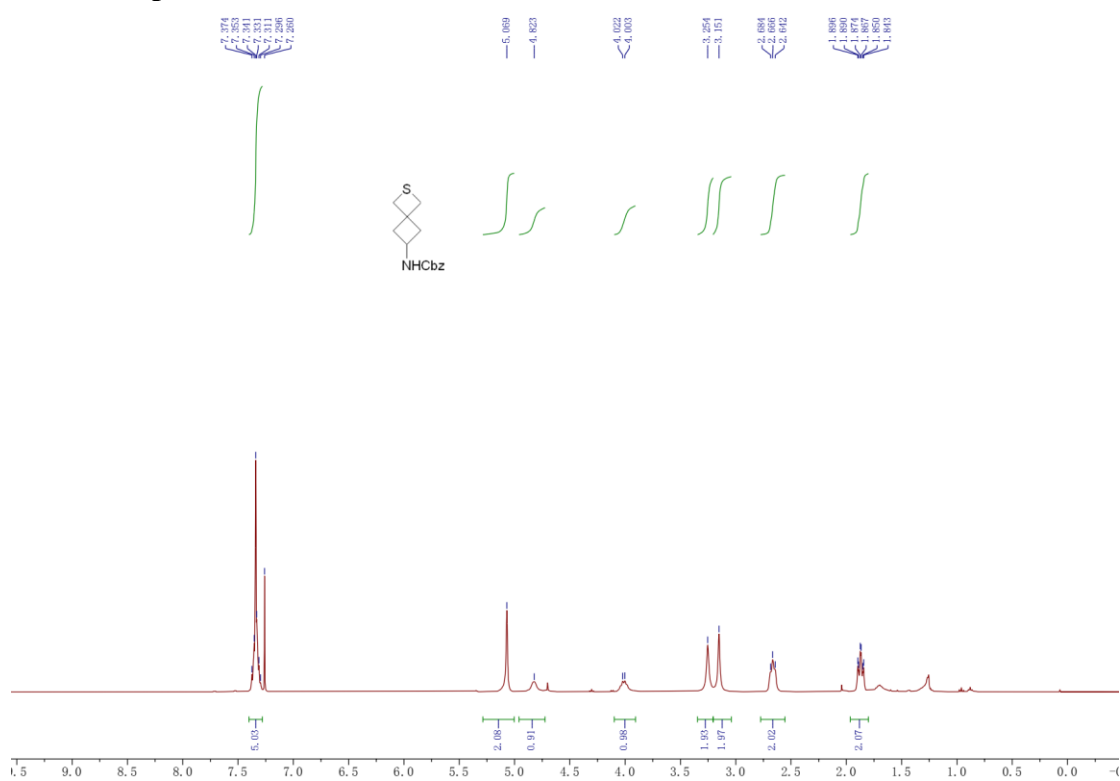
¹H NMR spectrum of 78



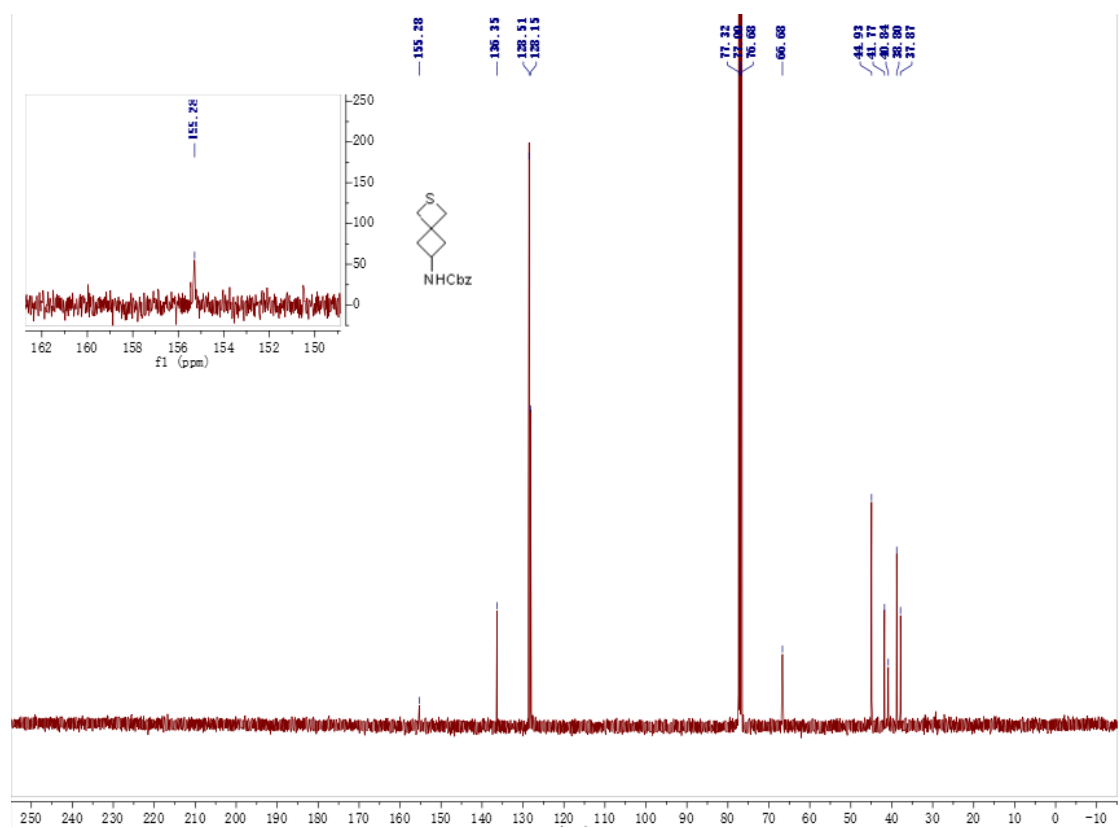
¹³C NMR spectrum of 78



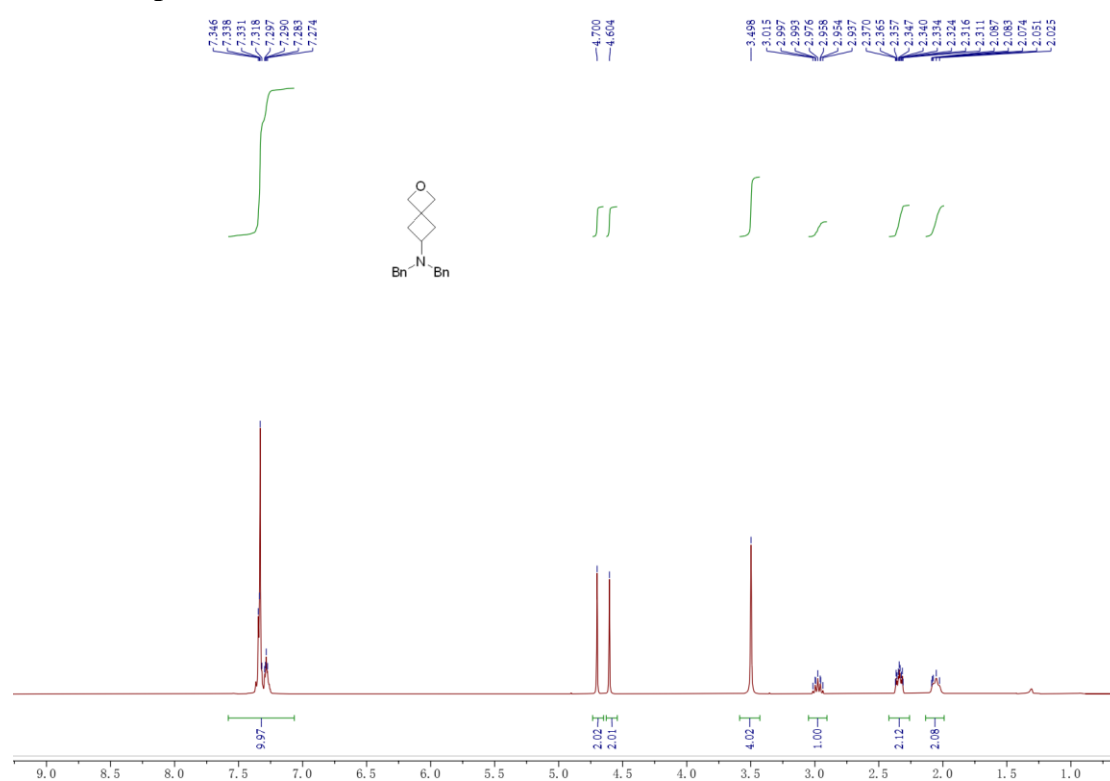
¹H NMR spectrum of 79



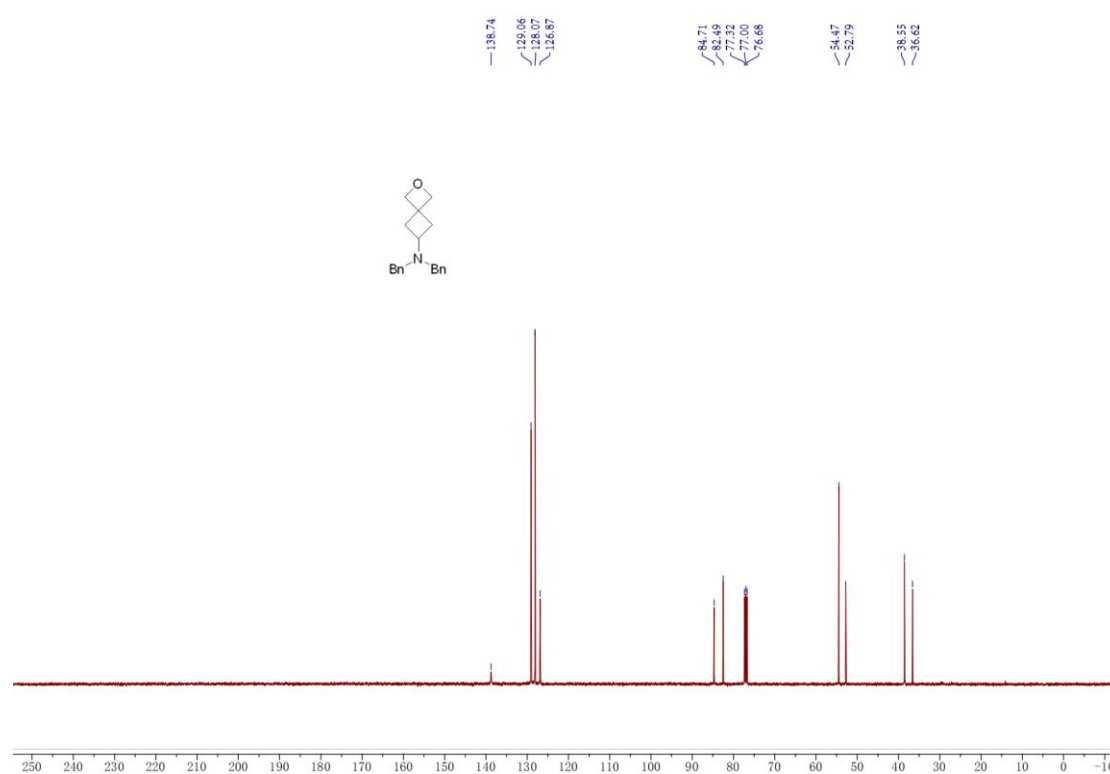
¹³C NMR spectrum of 79



¹H NMR spectrum of 1



¹³C NMR spectrum of 1

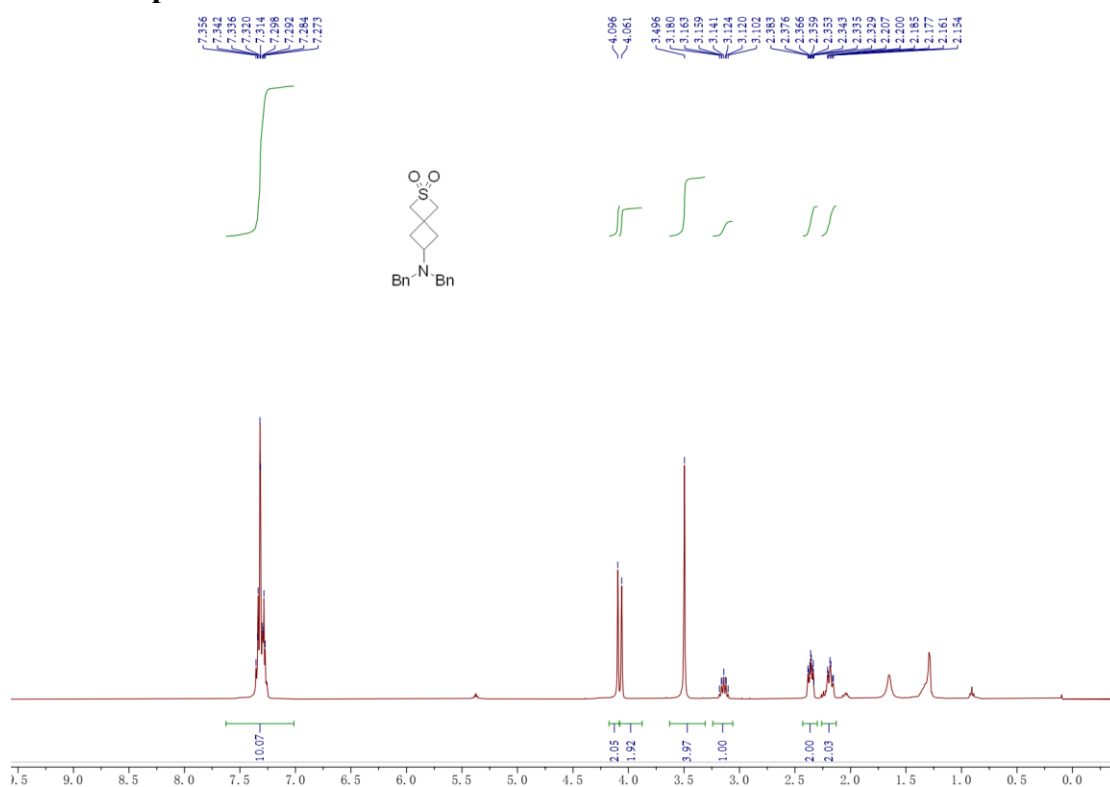


[illegible]

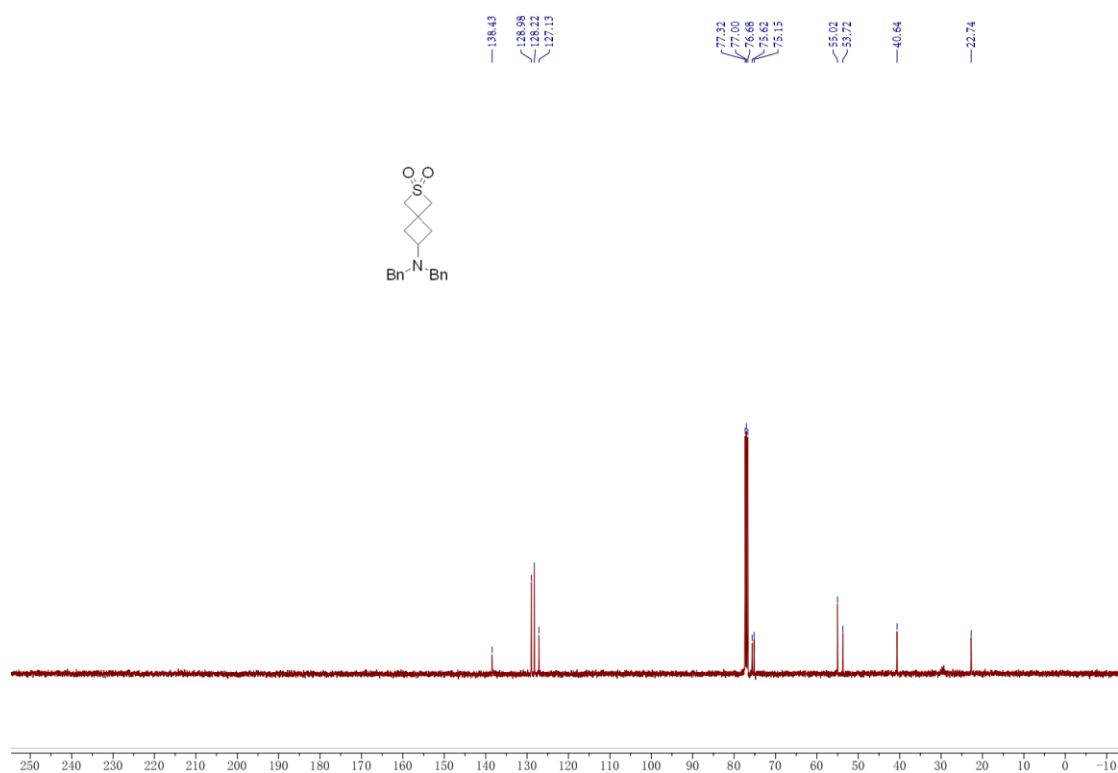
Chemical structure: C1CN(C1Cc2ccccc2)Cc3ccccc3

¹³C NMR peaks (ppm): 132.87, 129.09, 128.85, 77.21, 77.00, 76.79, 54.64, 52.46, 42.75, 41.61, 40.41, 38.20.

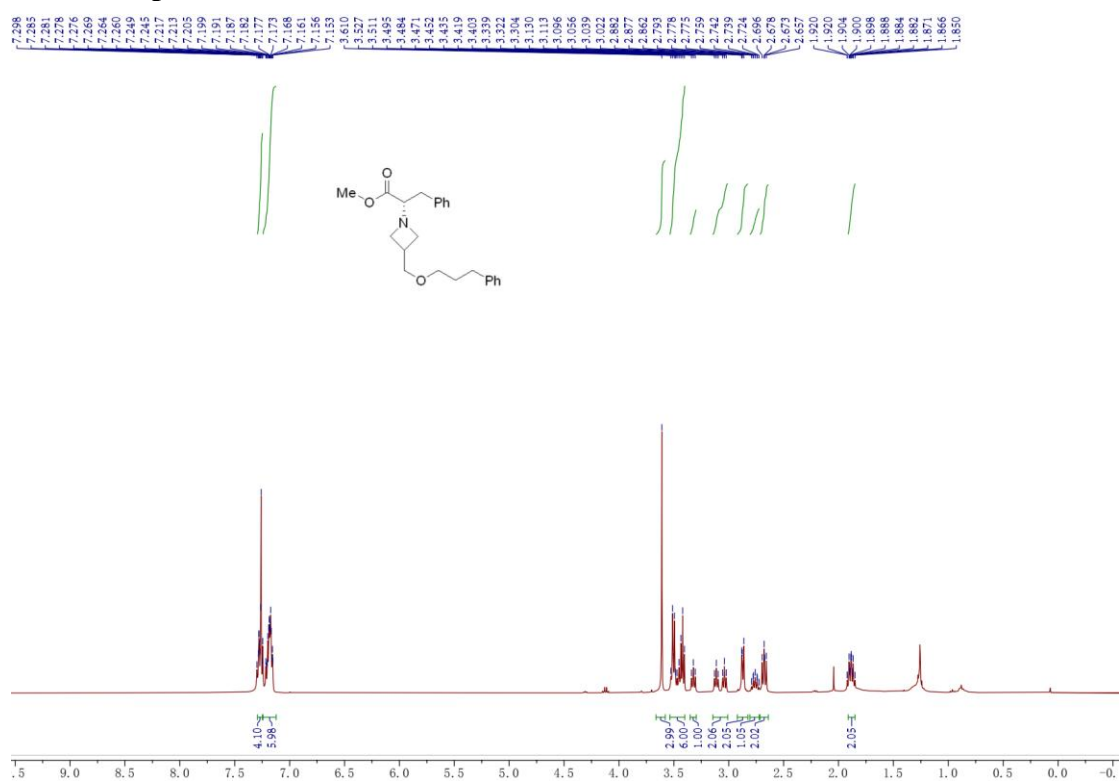
¹H NMR spectrum of 2



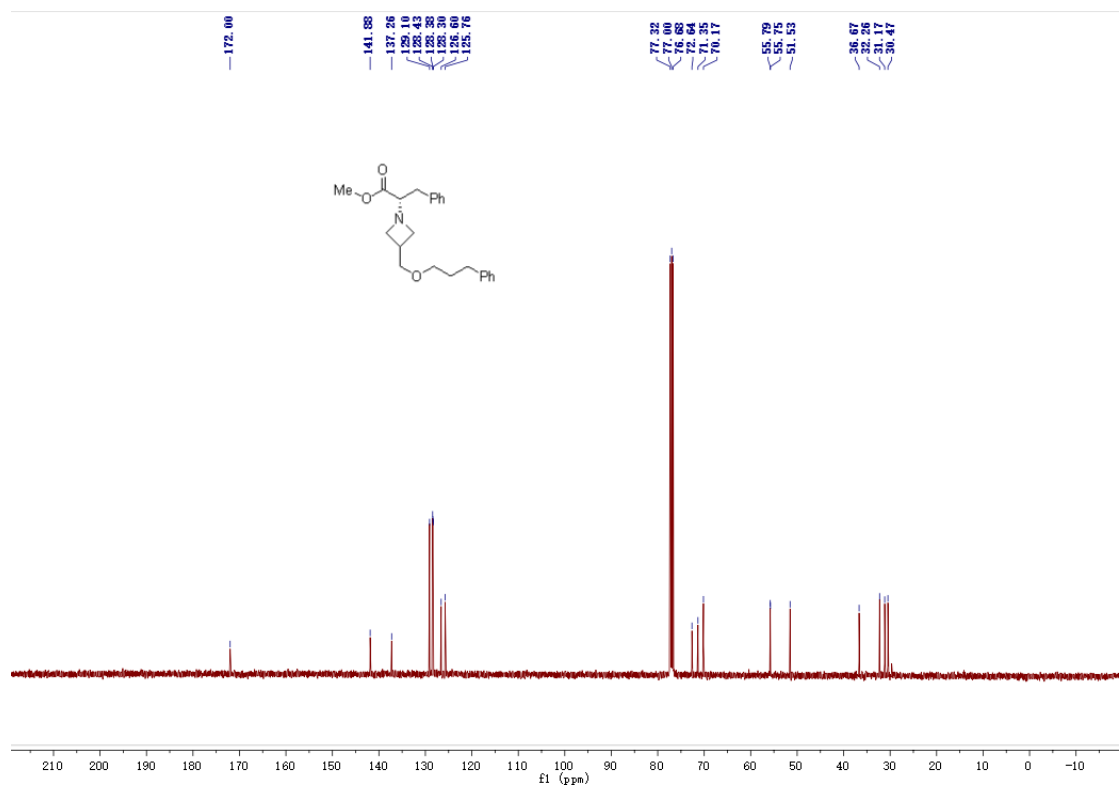
¹³C NMR spectrum of 2



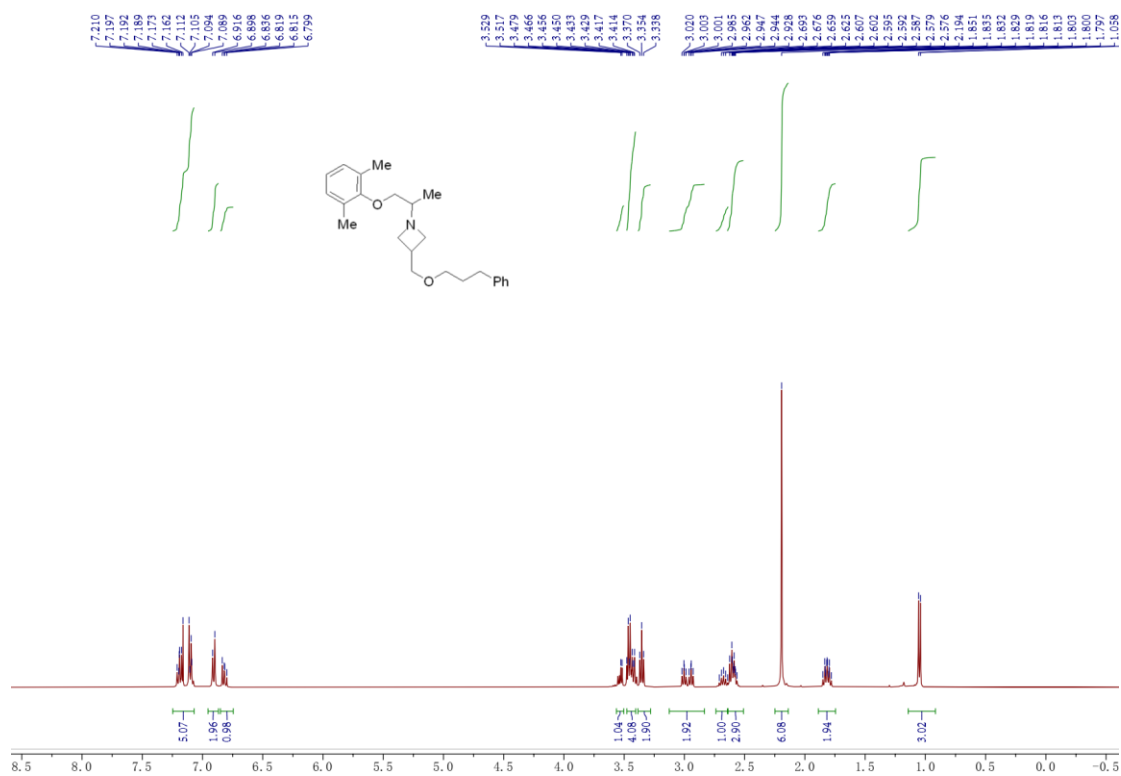
¹H NMR spectrum of 82



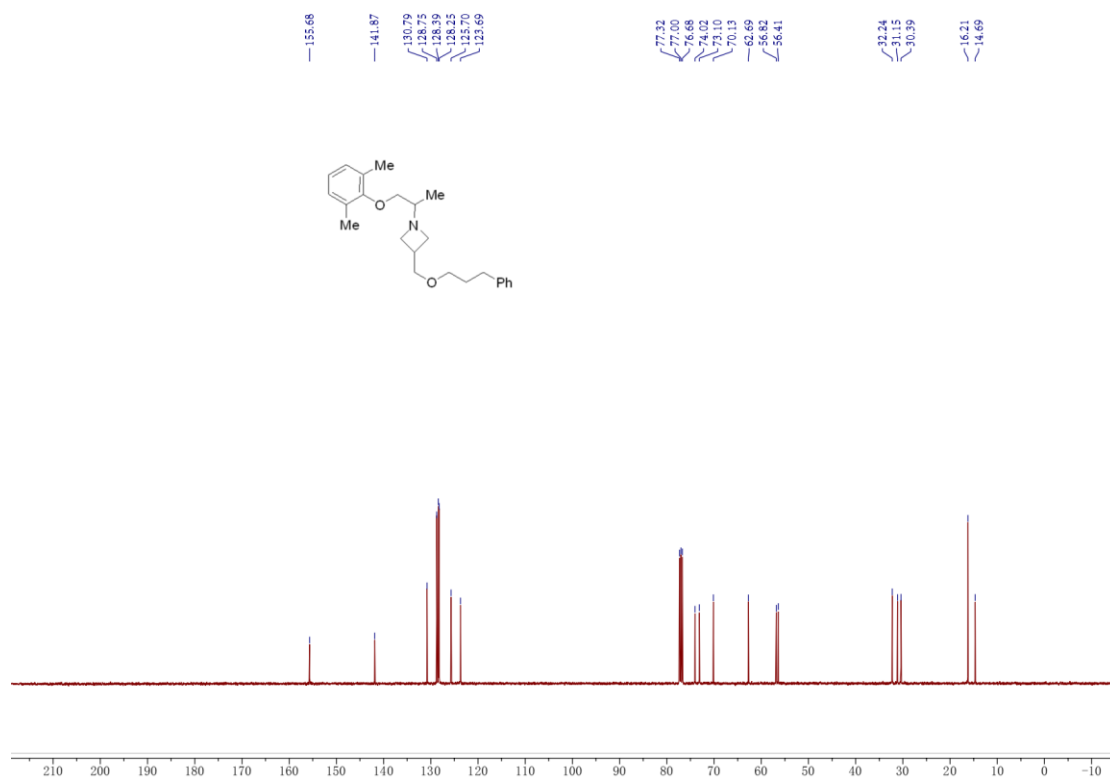
¹³C NMR spectrum of 82



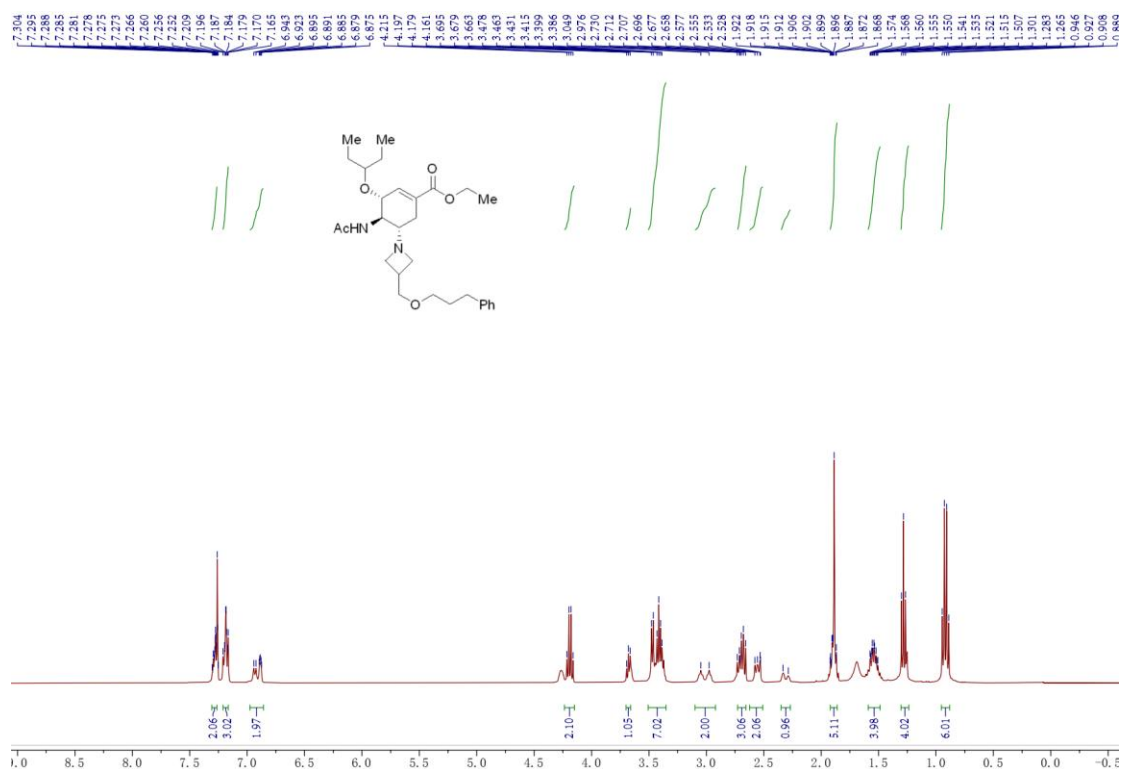
¹H NMR spectrum of 83



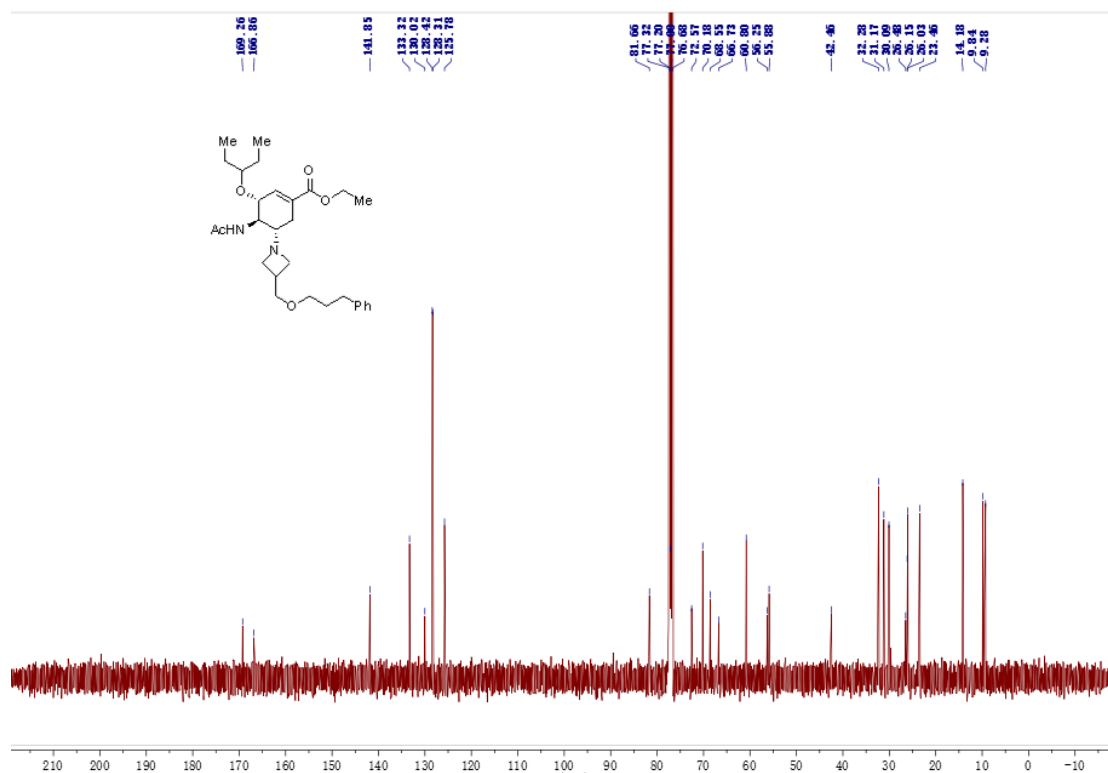
¹³C NMR spectrum of 83



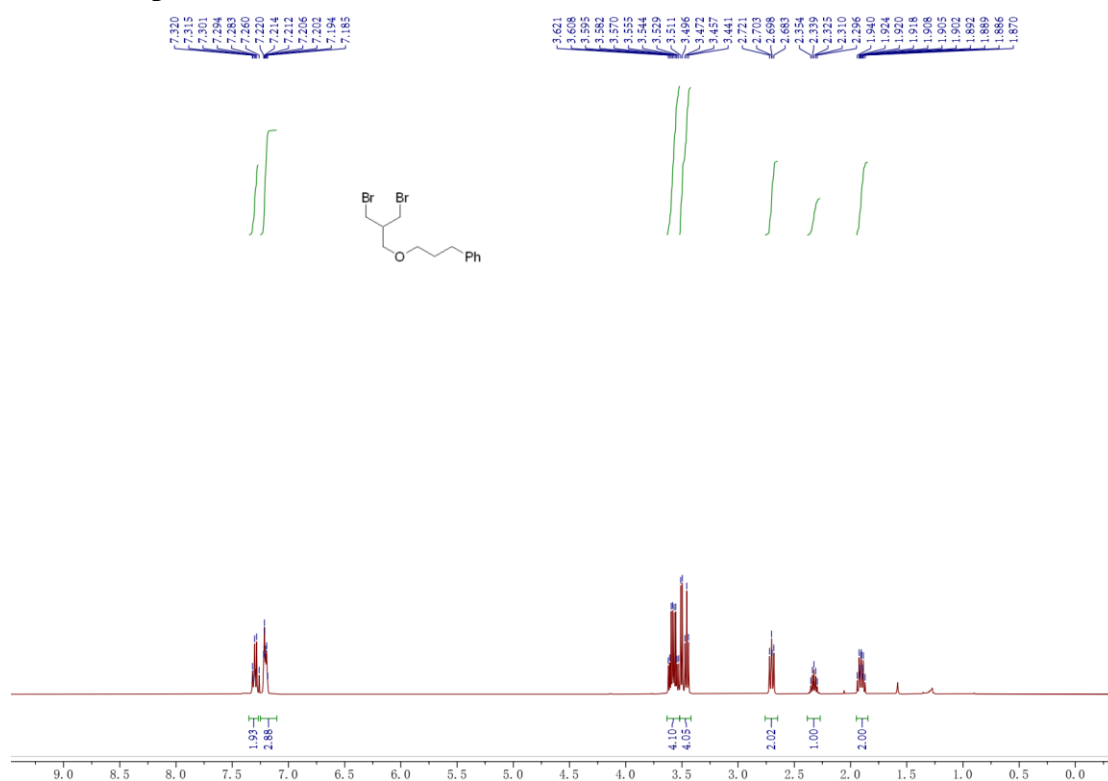
¹H NMR spectrum of 84



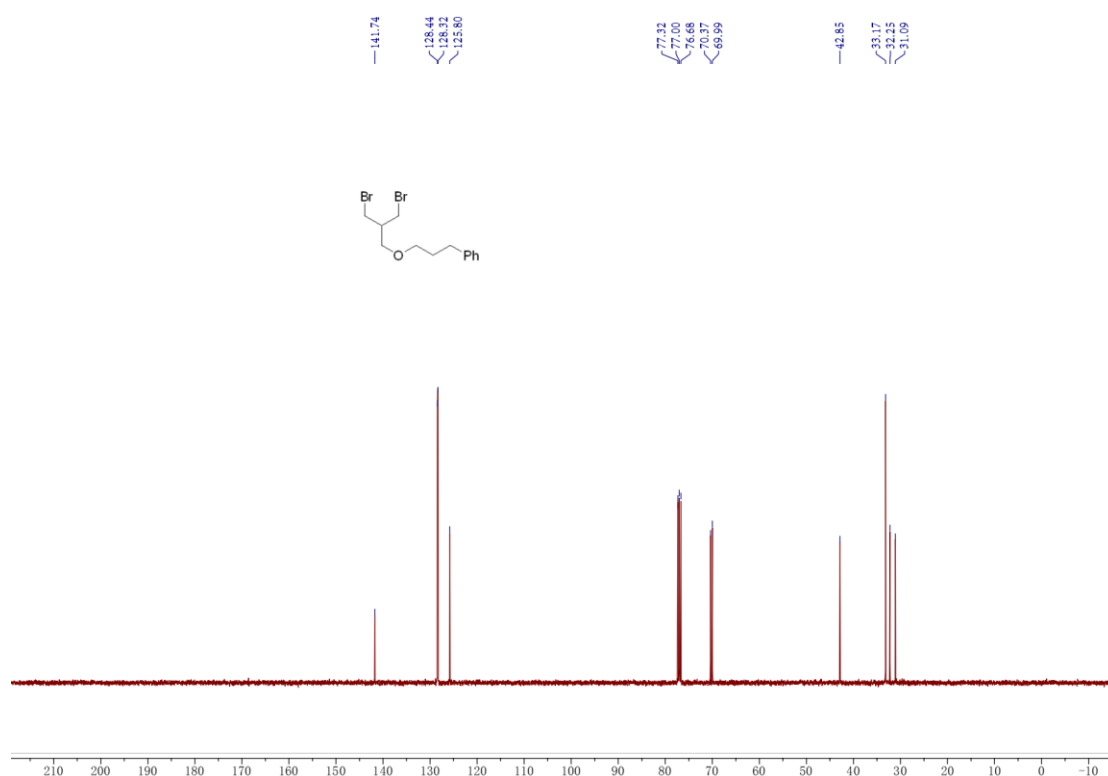
¹³C NMR spectrum of 84



¹H NMR spectrum of 10



¹³C NMR spectrum of 10



Chemical structure of 4-bromo-2-(4-phenoxybutyl)butanoic acid:

O=C(O)C(Br)CCOCCCC1=CC=CC=C1

¹H NMR spectrum (400 MHz, CDCl₃) showing peaks and integrations:

Chemical Shift (ppm)	Integration
~8.1	0.86
7.2-7.6	1.99, 2.50
~4.2	2.05
~3.5	6.01
~2.5	2.00
~2.0	1.00
~1.5	2.00

Chemical shift values (ppm) listed above the spectrum:

8.076, 7.365, 7.286, 7.207, 7.144, 7.104, 7.089, 7.174, 4.327, 4.313, 4.309, 4.295, 4.281, 4.265, 4.249, 4.233, 4.220, 4.204, 4.189, 4.174, 4.159, 4.144, 4.129, 4.113, 4.098, 4.083, 4.068, 4.053, 4.038, 4.023, 4.008, 3.993, 3.978, 3.963, 3.948, 3.933, 3.918, 3.903, 3.888, 3.873, 3.858, 3.843, 3.828, 3.813, 3.798, 3.783, 3.768, 3.753, 3.738, 3.723, 3.708, 3.693, 3.678, 3.663, 3.648, 3.633, 3.618, 3.603, 3.588, 3.573, 3.558, 3.543, 3.528, 3.513, 3.498, 3.483, 3.468, 3.453, 3.438, 3.423, 3.408, 3.393, 3.378, 3.363, 3.348, 3.333, 3.318, 3.303, 3.288, 3.273, 3.258, 3.243, 3.228, 3.213, 3.198, 3.183, 3.168, 3.153, 3.138, 3.123, 3.108, 3.093, 3.078, 3.063, 3.048, 3.033, 3.018, 2.998, 2.983, 2.968, 2.953, 2.938, 2.923, 2.908, 2.893, 2.878, 2.863, 2.848, 2.833, 2.818, 2.803, 2.788, 2.773, 2.758, 2.743, 2.728, 2.713, 2.698, 2.683, 2.668, 2.653, 2.638, 2.623, 2.608, 2.593, 2.578, 2.563, 2.548, 2.533, 2.518, 2.503, 2.488, 2.473, 2.458, 2.443, 2.428, 2.413, 2.398, 2.383, 2.368, 2.353, 2.338, 2.323, 2.308, 2.293, 2.278, 2.263, 2.248, 2.233, 2.218, 2.203, 2.188, 2.173, 2.158, 2.143, 2.128, 2.113, 2.098, 2.083, 2.068, 2.053, 2.038, 2.023, 2.008, 1.993, 1.978, 1.963, 1.948, 1.933, 1.918, 1.903, 1.888, 1.873, 1.858, 1.843, 1.828, 1.813, 1.798, 1.783, 1.768, 1.753, 1.738, 1.723, 1.708, 1.693, 1.678, 1.663, 1.648, 1.633, 1.618, 1.603, 1.588, 1.573, 1.558, 1.543, 1.528, 1.513, 1.498, 1.483, 1.468, 1.453, 1.438, 1.423, 1.408, 1.393, 1.378, 1.363, 1.348, 1.333, 1.318, 1.303, 1.288, 1.273, 1.258, 1.243, 1.228, 1.213, 1.198, 1.183, 1.168, 1.153, 1.138, 1.123, 1.108, 1.093, 1.078, 1.063, 1.048, 1.033, 1.018, 1.003, 0.988, 0.973, 0.958, 0.943, 0.928, 0.913, 0.898, 0.883, 0.868, 0.853, 0.838, 0.823, 0.808, 0.793, 0.778, 0.763, 0.748, 0.733, 0.718, 0.703, 0.688, 0.673, 0.658, 0.643, 0.628, 0.613, 0.598, 0.583, 0.568, 0.553, 0.538, 0.523, 0.508, 0.493, 0.478, 0.463, 0.448, 0.433, 0.418, 0.403, 0.388, 0.373, 0.358, 0.343, 0.328, 0.313, 0.298, 0.283, 0.268, 0.253, 0.238, 0.223, 0.208, 0.193, 0.178, 0.163, 0.148, 0.133, 0.118, 0.103, 0.088, 0.073, 0.058, 0.043, 0.028, 0.013, 0.000.

Chemical structure of 4-bromo-1-(4-phenylbutoxy)-2-(hydroxymethyl)ethyl acetate is shown above the spectrum.

¹H NMR spectrum (CDCl₃) of 4-bromo-1-(4-phenylbutoxy)-2-(hydroxymethyl)ethyl acetate. The spectrum shows peaks at 7.72, 7.70, 7.68, 7.65, 7.63, 7.62, 6.2, 4.7, 3.2, 3.17, 3.16, and 3.15 ppm. Integration values are provided for each peak.

Chemical Shift (ppm)	Integration
7.72	0.98
7.70	0.98
7.68	0.98
7.65	0.98
7.63	0.98
7.62	0.98
6.2	1.00
4.7	1.00
3.2	1.00
3.17	1.00
3.16	1.00
3.15	1.00

Chemical structure: BrCC(OC(=O)D)OCCCC1=CC=CC=C1

¹H NMR spectrum (CDCl₃) showing peaks from 0.0 to 8.0 ppm. Integration values are provided below the baseline: 1.89, 2.76, 2.02, 6.97, 1.96, 0.96, and 2.00. Chemical shift values are listed above the peaks.

Chemical structure of the compound is shown above the spectrum:

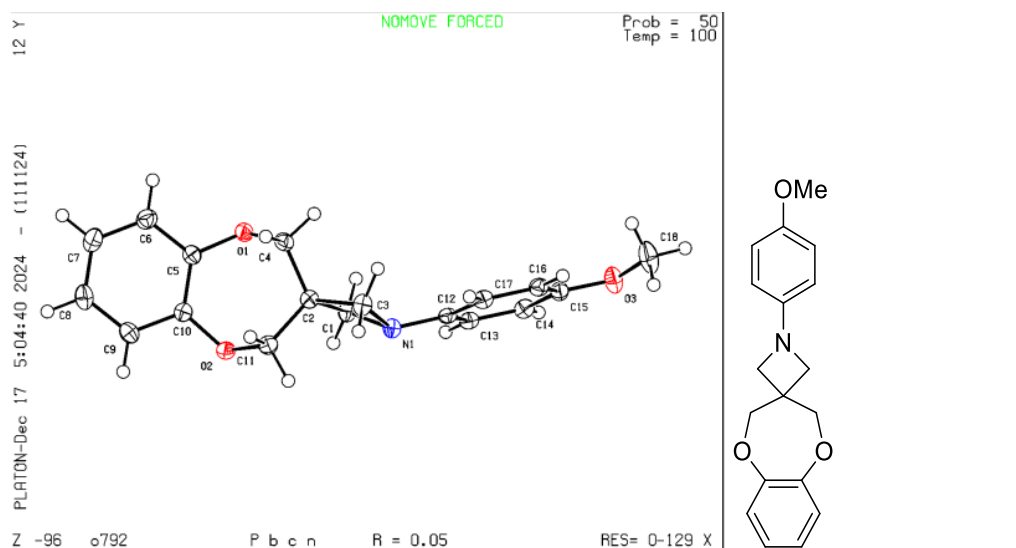
BrCCOC(=O)OCCOCCc1ccccc1

The spectrum displays several peaks corresponding to the chemical structure, with the following chemical shifts (ppm) labeled above the peaks:

- 141.77
- 128.45
- 128.33
- 128.81
- 77.32
- 77.00
- 76.08
- 70.41
- 68.80
- 62.78
- 40.44
- 32.24
- 31.85
- 31.08

The spectrum shows a complex pattern of peaks, with the most prominent peaks labeled above the spectrum. The peaks are distributed across the range from 31.08 to 141.77 ppm, with a significant peak at 77.00 ppm, likely representing the solvent (CDCl₃).

8. X-ray Crystallographic Data



Bond precision: C-C = 0.0018 Å

Wavelength=0.71073

Cell: a=18.4109(18)

b=6.6187(6)

c=25.243(2)

alpha=90

beta=90

gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	3076.0(5)	3076.0(5)
Space group	P b c n	P b c n
Hall group	-P 2n 2ab	-P 2n 2ab
Moiety formula	C18 H19 N O3	C18 H19 N O3
Sum formula	C18 H19 N O3	C18 H19 N O3
Mr	297.34	297.34
Dx, g cm ⁻³	1.284	1.284
Z	8	8
Mu (mm ⁻¹)	0.087	0.087
F000	1264.0	1264.0
F000'	1264.60	
h,k,lmax	25,9,35	25,9,35
Nref	4331	4329
Tmin,Tmax	0.983,0.990	0.683,0.727
Tmin'	0.983	

Correction method= # Reported T Limits: Tmin=0.683 Tmax=0.727
AbsCorr = MULTI-SCAN

Data completeness= 1.000

Theta(max)= 29.598

R(reflections)= 0.0472(3559)

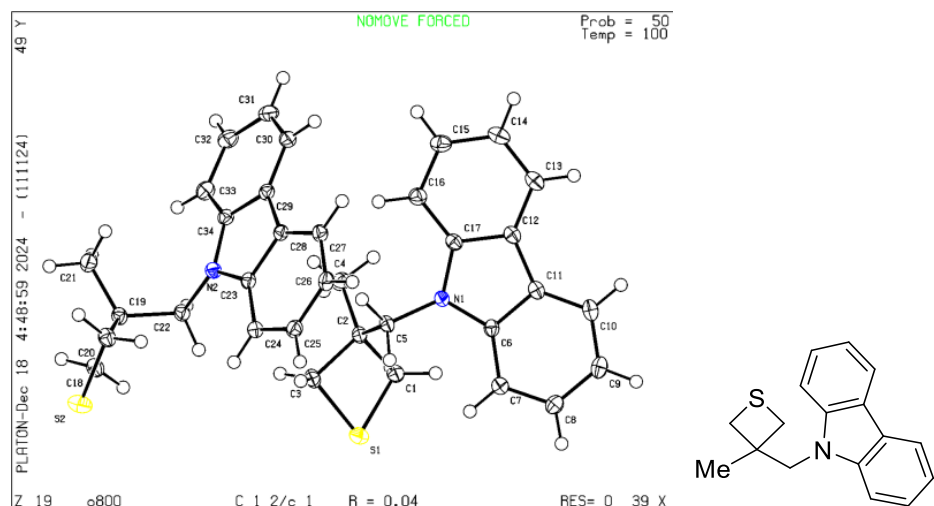
wR2(reflections)=
0.1126(4329)

S = 1.033

Npar= 200

Supplementary Figure 9. Crystal data and structure refinement for compound 23.

CCDC Number = 2446264



Bond precision: C-C = 0.0016 Å

Wavelength=0.71073

Cell: a=17.2318 (15)

b=11.0913 (10)

c=28.207 (3)

alpha=90

beta=91.991 (4)

gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	5387.8 (9)	5387.8 (9)
Space group	C 2/c	C 1 2/c 1
Hall group	-C 2yc	-C 2yc
Moiety formula	C17 H17 N S	C17 H17 N S
Sum formula	C17 H17 N S	C17 H17 N S
Mr	267.38	267.37
Dx, g cm ⁻³	1.319	1.319
Z	16	16
Mu (mm ⁻¹)	0.225	0.225
F000	2272.0	2272.0
F000'	2274.67	
h, k, lmax	24, 15, 40	24, 15, 40
Nref	8295	8265
Tmin, Tmax	0.936, 0.947	0.711, 0.742
Tmin'	0.936	

Correction method= # Reported T Limits: Tmin=0.711 Tmax=0.742

AbsCorr = MULTI-SCAN

Data completeness= 0.996

Theta(max)= 30.570

R(reflections)= 0.0386 (7273)

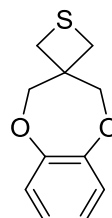
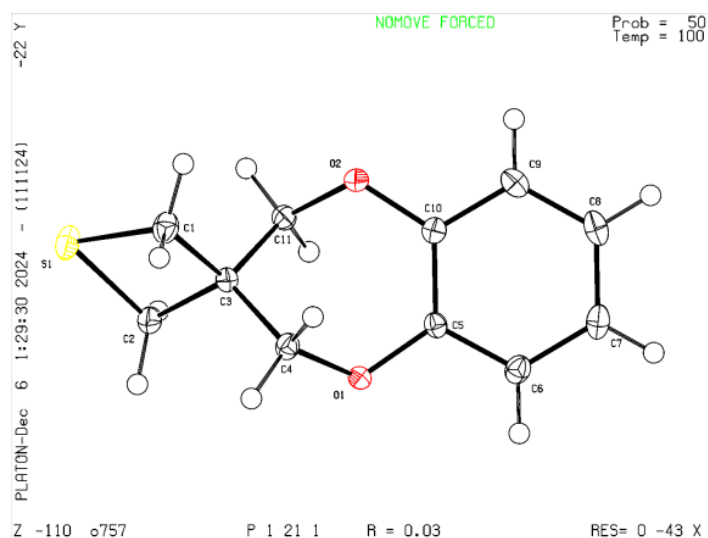
wR2(reflections)=
0.1041 (8265)

S = 1.060

Npar= 345

Supplementary Figure 10. Crystal data and structure refinement for compound 49.

CCDC Number = 2446104



Bond precision: C-C = 0.0028 Å Wavelength=0.71073

Cell: a=6.1003 (4) b=6.9680 (4) c=11.8794 (6)
alpha=90 beta=104.158 (2) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	489.62 (5)	489.62 (5)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C11 H12 O2 S	C11 H12 O2 S
Sum formula	C11 H12 O2 S	C11 H12 O2 S
Mr	208.27	208.27
Dx, g cm ⁻³	1.413	1.413
Z	2	2
Mu (mm ⁻¹)	0.299	0.299
F000	220.0	220.0
F000'	220.34	
h, k, lmax	8, 9, 16	8, 9, 16
Nref	2770 [1493]	2736
Tmin, Tmax	0.947, 0.971	0.713, 0.746
Tmin'	0.946	

Correction method= # Reported T Limits: Tmin=0.713 Tmax=0.746
AbsCorr = MULTI-SCAN

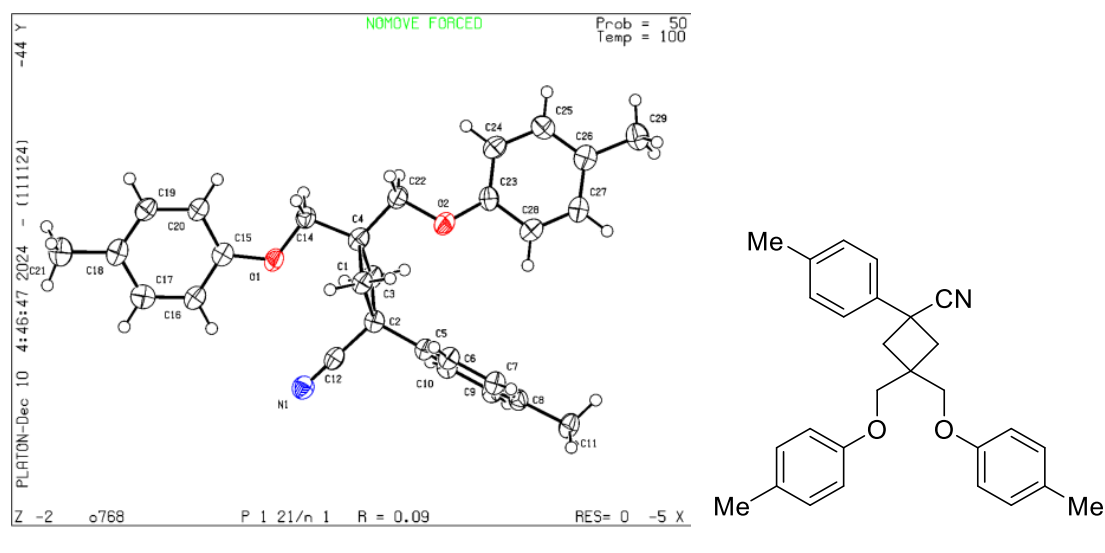
Data completeness= 1.83/0.99 Theta(max)= 29.582

R(reflections)= 0.0269 (2693) wR2(reflections)=
0.0669 (2736)

S = 1.062 Npar= 127

Supplementary Figure 11. Crystal data and structure refinement for compound 51.

CCDC Number = 2446091



Bond precision: C-C = 0.0059 Å Wavelength=1.54178

Cell: a=6.0027 (2) b=15.1694 (5) c=24.8925 (9)
alpha=90 beta=93.445 (2) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2262.55 (13)	2262.55 (13)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C ₂₈ H ₂₉ N O ₂	C ₂₈ H ₂₉ N O ₂
Sum formula	C ₂₈ H ₂₉ N O ₂	C ₂₈ H ₂₉ N O ₂
Mr	411.52	411.52
Dx, g cm ⁻³	1.208	1.208
Z	4	4
Mu (mm ⁻¹)	0.586	0.586
F ₀₀₀	880.0	880.0
F ₀₀₀ '	882.42	
h, k, lmax	7, 18, 29	7, 18, 29
Nref	4000	3990
Tmin, Tmax	0.951, 0.961	0.633, 0.753
Tmin'	0.920	

Correction method= # Reported T Limits: Tmin=0.633 Tmax=0.753
AbsCorr = MULTI-SCAN

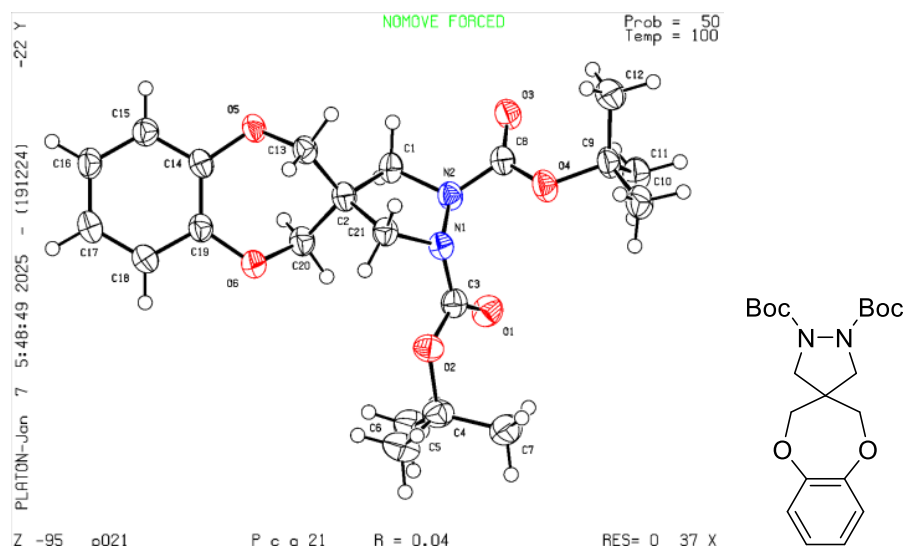
Data completeness= 0.998 Theta(max)= 66.814

R(reflections)= 0.0875 (3474) wR2(reflections)=
0.2523 (3990)

S = 1.118 Npar= 283

Supplementary Figure 12. Crystal data and structure refinement for compound 61.

CCDC Number = 2446094



Bond precision: C-C = 0.0045 Å Wavelength=1.54178

Cell: a=19.4245 (8) b=17.2635 (7) c=6.3969 (3)
alpha=90 beta=90 gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2145.10 (16)	2145.10 (16)
Space group	P c a 21	P c a 21
Hall group	P 2c -2ac	P 2c -2ac
Moiety formula	C ₂₁ H ₃₀ N ₂ O ₆	C ₂₁ H ₃₀ N ₂ O ₆
Sum formula	C ₂₁ H ₃₀ N ₂ O ₆	C ₂₁ H ₃₀ N ₂ O ₆
Mr	406.47	406.47
Dx, g cm ⁻³	1.259	1.259
Z	4	4
Mu (mm ⁻¹)	0.760	0.760
F ₀₀₀	872.0	872.0
F ₀₀₀ '	874.82	
h, k, lmax	23, 21, 7	23, 21, 7
Nref	4101 [2252]	4072
Tmin, Tmax	0.919, 0.949	0.607, 0.753
Tmin'	0.840	

Correction method= # Reported T Limits: Tmin=0.607 Tmax=0.753
AbsCorr = MULTI-SCAN

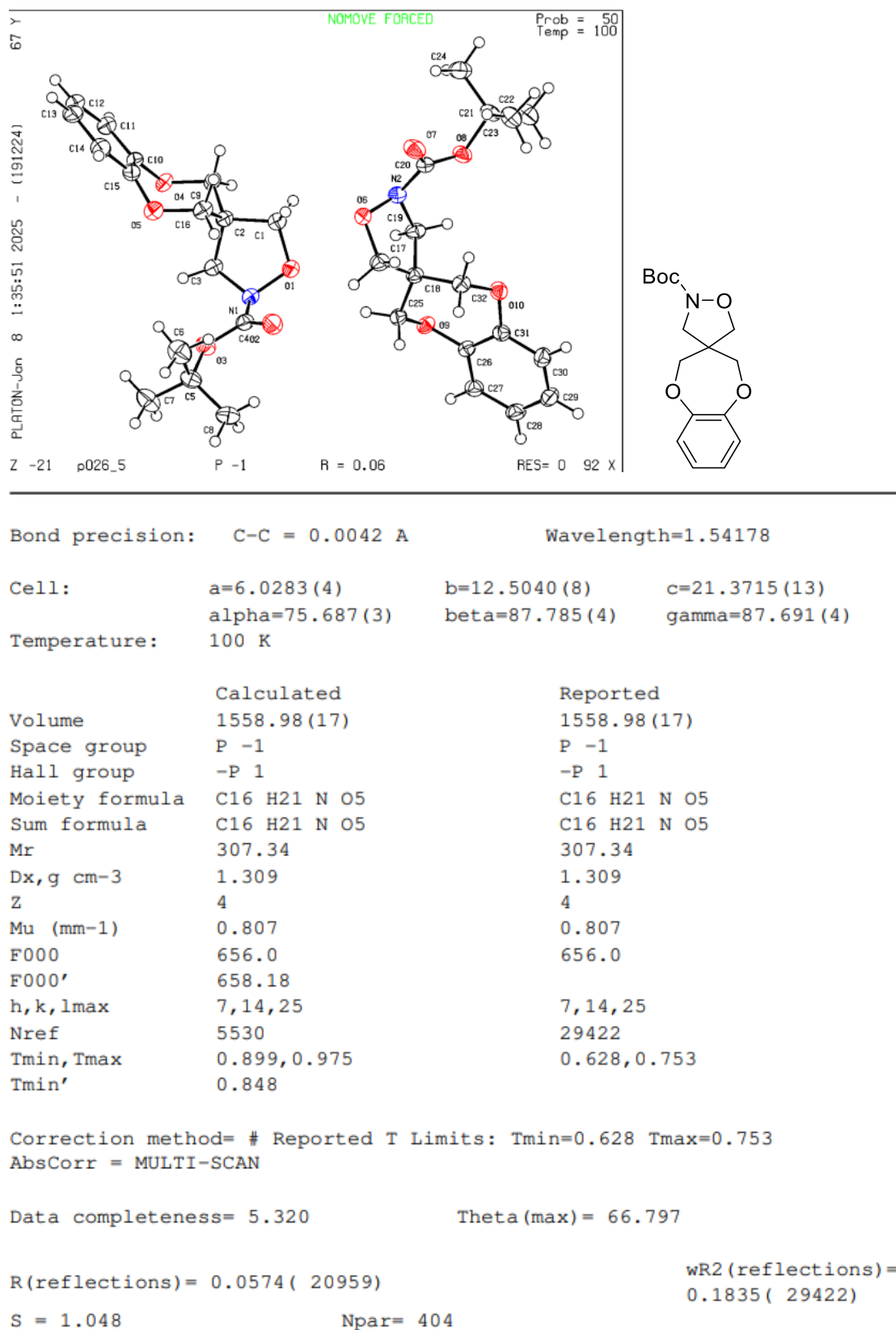
Data completeness= 1.81/0.99 Theta(max)= 70.392

R(reflections)= 0.0405 (3582) wR2(reflections)=
0.1058 (4072)

S = 1.048 Npar= 268

Supplementary Figure 13. Crystal data and structure refinement for compound 66.

CCDC Number = 2446107



Supplementary Figure 14. Crystal data and structure refinement for compound 67.

CCDC Number = 2446108

9. References

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